L13: Entry 3 of 4 File: USPT Jun 27, 1995

DOCUMENT-IDENTIFIER: US 5428163 A
TITLE: Prodrugs for selective drug delivery

Detailed Description Text (84):
A cellular and blood-brain barrier permeant luminide comprising a C functionality of a cellular and blood-brain barrier impermeant inhibitor of catechol-o-methyltrasferase such as 3,5-diiodo-4-hydroxybenzoic acid, S-3'-deoxyadenosylLhomocysteine, pyrogallol, R04-4602, gallic acid, 3,5-dihydroxy-4-methylbenzoic acid, 1,3-dihydroxy-2-methoxybenzene, 1-hydroxy-2,3-dimethoxybenzene, 2-hydroxy-1,3-dimethoxybenzene, 1,3-dihydroxy-4-methoxybenzene, catechol, 3,4-dihydroxybenzoic acid, caffeic acid, 5,6-dihydroxyindole, noradnamine, dopacetamide, H 22/54, quercetin, nordihydroguaiaretic acid, U-0521, arterenone, methylspinazarin, MK 486, dopa, papaveroline, isoprenaline, 7,8-dihydroxychlorpromazine, 3-hydroxy-4-pyridone, tetrahydroisoquinoline pyridoxal 5'-phosphate, iodoacetic acid, 3-mercaptotyramine, dehydrodicaffeic acid dilactone, methylspinazorin, 3',5,7-trihydroxy-4',6-dimethoxyisoflavone, 3',5,7-trihydroxy- 4',8-dimethoxyisoflavone, 6,7-dihydromethylspinazarin, S-adenosylhomocysteine, S-tubercidinylhomocysteine, 3',8-dihydroxy-4',6,7-trimethoxyisoflavone,7-0-methylspinochrome B, 6-(3-hydroxybutyl)-7-0-methylspinachrome B, 3,5-diiodosalicyclic acid, or pyridoxal-5'-phosphate is an antidepressant agent which increases brain levels of monoamines and is an agent to block the metabolism of L-dopa administered for the treatment of Parkinsonism.

DOCUMENT-IDENTIFIER: US 5451519 A
TITLE: Cloning restriction endonuclease genes by modulating methyltransferase activity

Brief Summary Text (3):
Restriction endonucleases originally were identified by studying the inability of bacteriophage from strains of E. coli to infect other strains of E. coli. (Dussoix and Arber, J. Mol. Biol. 5: 37 (1962)). It now is well established that this phenomena, called restriction, is mediated by two types of enzymes, which are called restriction endonucleases and DNA methyltransferases.

Brief Summary Text (27):
The method has been demonstrated only in a model system. In this example, a clone encoding the HaeIII methyltransferase was introduced into an E. coli host temperature sensitive for mcrB, a methylation dependent endonuclease of the E. coli mcr restriction system. (The E. coli mcr and mrr digest DNA methylated at specific sequences, as described in Raleigh et al., Proc. Nat'l. Acad. Sci., 83: 9070 (1986) and Dila et al., J. Bac. 172: 4888 (1990)). Transformed host cells were grown initially under permissive conditions at 42.degree. C., where mcrB is inactive, providing for expression of the HaeIII methyltransferase and resultant methylation of the host DNA. Then, replicates were grown at the non-permissive temperature, 30.degree. C., where mcrB is active. Under non-permissive conditions at 30.degree. C., the mcrB endonuclease degraded host DNA methylated by the HaeIII methyltransferase causing the death of cells that expressed this gene. The method suffers from the drawbacks of other methods that select for the methyltransferase.

Brief Summary Text (40):
In accordance with still another aspect of the claimed invention there are provided host cells for detecting DNA damage. In a preferred embodiment of this aspect of the invention the host cells do not efficiently repair DNA damage by a restriction endonuclease. Highly preferred embodiments in this aspect of the invention are DNA ligase deficient cells. Particularly preferred cells are E. coli cells that are lig4, lig7 or lig4 and lig7 deficient cells.

Brief Summary Text (41):
In another embodiment of this aspect of the invention there are provided host cells that do not express a restriction-modification system that degrades methylated DNA. Preferred E. coli hosts in this aspect of the invention are mcrA, mcrB, mcrC, mcrD, mcrE, mcrF or mrr deficient.

Brief Summary Text (48):
In a further aspect of the invention there is provided host cells that comprise (A) a first exogenously-derived inducible promoter not controlled by the cellular effects of DNA damage operably linked to a first exogenously-derived gene that encodes a protein for modulating the intracellular concentration of

S-adenosyl-L-methionine, and (B) a second exogenously-derived promoter which is regulated by the cellular effects of restriction endonuclease-mediated DNA damage operably linked to a second exogenously-derived gene that encodes a reporter protein, wherein (C) inducing the first promoter modulates the intracellular concentration of S-adenosyl-L-methionine and restriction endonuclease-mediated DNA damage is determined by the reporter protein. A very highly preferred host for use in this aspect of the invention is E. coli GUBCE-1.

Brief Summary Text (50):
In yet another aspect of the invention there is provided isolated, purified DNA comprising a region encoding a cognate methyltransferase and restriction endonuclease obtained by a method comprising the step of modulating the cellular concentration of a methyl donor cofactor of a methyltransferase to detect the presence of an exogenously derived DNA encoding said restriction endonuclease in a host. In certain highly preferred embodiments of this aspect of the invention isolated, purified DNA is obtained by a method in which the concentration of S-adenosyl-L-methionine is controlled by chlortetracycline induced expression of a bacteriophage T3 S-adenosyl-L-methionine hydrolase gene operably linked to a TN10 tetracycline promoter and the presence of a gene encoding a restriction endonuclease is determined by SOS-induced expression of a .beta.-galactosidase gene operably linked to the E. coli dinD1 promoter.

Detailed Description Text (16):
An important aspect of the invention is the host for expressing DNA from a restriction enzyme source organism. Practically any organism can be used in the invention. Suitable hosts thus include E. coli, B. subtilis, yeast, insect and mammalian cells, to name just a few.

Detailed Description Text (18):
For instance, preferred hosts do not express an endogenous methyltransferase activity that adversely affects cellular growth in the presence of low cellular concentrations of the methyl donor co-factor. Thus, for example, preferred E. coli hosts are dam. E. coli cells of this genotype do not express the E. coli DNA adenine methyltransferase, which regulates DNA replication. This enzyme methylates newly replicated DNA. Low cellular concentrations of the methyl donor co-factor S-adenosyl-L-methionine inhibit the activity of the enzyme leading to the production in the cell of hemimethylated DNA in the host. Hemimethylated DNA is not well replicated by E. coli. Therefore, low cellular concentration of S-adenosyl-L-methionine inhibits cell growth, which can interfere with some assays useful in the invention to detect the presence of the cloned restriction endonuclease. Thus, E. coli hosts for use in the invention are preferably dam. The dam system and E. coli mutants in this system are described in Landoulsi et al., Cell 63: 1053 (1990), for instance, herein incorporated by reference in its entirety.

Detailed Description Text (20):
For example, systems of this type have been described in E. coli. Genotypically the methylation dependent enzymes are referred to as mcrA, mcrB, mcrC, mcrD, mcrE, mcrF and mrr, as described in Raleigh et al., J. Bac. 173: 2707 (1991), for instance, also herein incorporated by reference in its entirety. Accordingly, E. coli deficient in mcrA, mcrB, mcrC, mcrD, mcrE, mcrF and mrr are preferred E. coli hosts.

Detailed Description Text (22):
In E. coli, repair of this type is mediated by the genes lig4 and lig7, which encode DNA ligases. To prevent repair of double strand breaks that will interfere with detecting a cloned restriction endonuclease gene expressed in E. coli host, preferred E. coli host for use in the invention include lig4, lig7 and lig4 and lig7 deficient stains of E. coli. Mutations in these genes are described in Konrad et al., J. Mol. Biol. 77:519 (1973) and Gottesman et al., J. Mol. Biol. 77:531 (1973), for example, herein incorporated by reference in their entirety.

Detailed Description Text (35):
Preferred promoters for use in accordance with the invention are tightly controlled inducible promoters that exhibit inducer dose dependent induction. With promoters of this type expression of enzymes that affect the cellular concentration of S-adenosyl-L-methionine can be adjusted to the optimum balance of the deleterious effect of low S-adenosyl-L-methionine on the host and sensitivity to the effects of DNA damage by a cloned restriction endonuclease. Particularly preferred promoters include the E. coli lac, mac, trp, tac, and trc promoters and the Tn10 tet promoter.

Detailed Description Text (38):
Highly preferred among those enzymes that affect S-adenosyl-L-methionine synthesis are the S-adenosyl-methionine synthetases, particularly the E. coli metK gene product.

Detailed Description Text (39):
Highly preferred among enzymes that degrade S-adenosyl-L-methionine are the enzymes S-adenosyl-L-methionine hydrolase, aminocyclopropane-1-carboxylic acid synthase and S-adenosyl-L-methionine decarboxylase. Particularly preferred among these enzymes is the T3 S-adenosyl-L-methionine hydrolase (also called SAMase) and the S-adenosyl-L-methionine decarboxylase product of the E. coli Sped gene.

Detailed Description Text (43):
Preferred embodiments of this aspect of the invention, therefore, inducibly express the E. coli metK gene. The gene has been cloned. A temperature-sensitive mutant of the cloned gene has been generated. And, furthermore, a host cell strain has been derived in which the temperature sensitive gene has replaced the endogenous gene. This work is described in Hafner et al., J. Bac. 132:832 (1977) and Satishchandran et al., J. Bac., 172 4489 (1990), herein incorporated by reference in their entirety.

Detailed Description Text (54):
E. coli SOS-sensitive transcriptional regulatory regions that are sensitive to effects engendered by double-strand DNA breaks and are suitable for use in the invention include but are not limited to promoters of the dinA, dinB, dinD, dinF, dinG, dinH, dinR, dinY, DDB, DRP, gadd153, PHR1, and RAD2 genes. Among these promoters the promoter of the dinD gene is particularly preferred because it is highly induced by DNA damage.

Detailed Description Text (58):
Hosts deficient in the genes that repair DNA damage caused by restriction endonucleases are preferred hosts for use in the invention, as described above. Such hosts are more sensitive to the deleterious effect of the restriction endonuclease. In E. coli, host cells deficient in lig4 or lig7 or both are preferred for use in the invention. Because they are unable to repair DNA damage, growth of these cells is more sensitive to the double-strand DNA breaks made by the restriction endonucleases. Moreover, deficiencies in these genes also can augment induction of the SOS response by restriction endonuclease-mediated DNA damage.

Detailed Description Text (85):
To demonstrate that S-adenosyl-L-methionine hydrolase could be used to control cellular DNA methylation pGUBC-2080 was introduced into E. coli 3055 cells (described below) together with pMBamHII, a plasmid that constitutively expresses a BamHII methyltransferase. pMBamHII is described in Connaughton et al., Nuc. Acids Res. 18:4002 (1990).

Detailed Description Text (90):
Construction of a dam.sup.- E. coli strain that expresses .beta.-galactosidase in response to DNA damage.

Detailed Description Text (91):
In accordance with the foregoing discussion an E. coli strain was constructed which provides a convenient colorimetric assay for cellular DNA damage. It is well known that the dam methyltransferase inhibits plasmid and host cell replication by producing hemimethylated DNA, as described in Zinder et al., Cell 20: 1071 (1987). To avoid this problem the stain was constructed from a dam.sup.- strain of E. coli. The experiments in this example employed the dam.sup.- E. coli strain 3055, which is a dam.sup.- derivative of the well known and readily available E. coli strain MC1061. The method used to make 3055 from MC1061 are well known to those of skill and readily can be employed to make dam.sup.- derivatives not only of MC1061 but practically any other strain of E. coli. MC1061 has been deposited in the ATCC by Hoffman LaRoche under accession number 53338.

Detailed Description Text (92):
The JH139 strain of E. coli contains a dinD .beta.-galactosidase fusion in which the dinD promoter operator controls expression of .beta.-galactosidase, as described in Heitman et al., Gene 103: 1 (1991), herein incorporated by reference in its entirety. Also as described in Heitman, the same fusion contains a kanamycin resistance gene. JH139 thus was a particularly convenient source of an SOS-inducible .beta.-galactosidase gene to indicate cellular DNA damage by a restriction endonuclease. Of course, many other constructs might be employed for this purpose, as described above.

Other Reference Publication (6):
Mann et al.,"Cloning Of Restriction And Modification Genes In E. Coli: The Hhall System From Haemophilus Haemolyticus", Gene, vol. 3:97-112, (1978).

Other Reference Publication (8):
Takiff et al., "Genetic Analysis Of The rnc Operon Of Escherichia coli", Journal of Bacteriology, vol. 171:2581-2590, (1989).

Other Reference Publication (9):
C. Satishchandran et al., "Novel Escherichia coli K-12 Mutants Impaired In S-Adenosylmethionine Synthesis", Journal Of Bacteriology, vol. 172:4489-4496, (1990).

Other Reference Publication (11):
Landoulsi et al., "The E. coli Cell Surface Specifically Prevents The Initiation of DNA Replication At oriC On Hemimethylated DNA Templates", Cell, vol. 63:1053-1060, (1990).

Other Reference Publication (12):
Russell et al., "Hemimethylation Prevents DNA Replication In E. coli", Cell, vol. 50:1071-1079, (1987).

Other Reference Publication (13):
Lewis et al., "Isolation Of DNA Damage-Inducible Promoters In Escherichia coli: Regulation Of polB (dinA), dinG, and dinH by LexA Repressor", Journal of Bacteriology, vol. 174:3377-3385, (1992).

Other Reference Publication (21):
Petit et al., "Characterization Of din Y, a New Escherichia coli DNA Repair Gene Whose Products Are Damage Inducible Even in a lex(Def) Background", Journal of Bacteriology, vol. 175:642-646, (1993).

Other Reference Publication (23):
Piekarowicz et al., "Isolation Of Temperature-Sensitive McrA and McrB Mutations An Complementation Analysis Of The McrBC Region Of Escherichia coli K-12", Journal of Bacterilogy, vol. 173:150-155, (1991).

Other Reference Publication (25):
Hughes et al., "Expression Of The Cloned Coliphage T3 S-Adenosylmethionine Hydrolase Gene Inhibits DNA Methylation And Polyamine Biosynthesis in Escherichia coli", Journal of Bacterilolgy, vol. 169:3625-3632, (1987).

Other Reference Publication (27):
Little et al., "The SOS Regulatory System Of Escherichia coli", Cell, vol. 29:11-22, (1982).

CLAIMS:

33. A host cell according to claim 32, wherein said cell is E. coli GUBCE-1.

40. An isolated, purified DNA according to claim 39, wherein in said method the concentration of S-adenosyl-L-methionine in said cells under said first and second growth conditions is determined by chlortetracycline induced expression of a bacteriophage T3 S-adenosyl-L-methionine hydrolase gene operably linked to a TN10 tetracycline promoter and the presence of a gene encoding a restriction endonuclease is determined by SOS-induced expression of a .beta.-galactosidase gene operably linked to an E. coli dinD1 promoter.

DOCUMENT-IDENTIFIER: US 5270178 A

**** See image for Certificate of Correction ****

TITLE: Vectors and compounds for expression of zymogen forms of human protein C

Brief Summary Text (15):

The DNA sequence depicted above was derived from cDNA clones prepared from human liver mRNA that encodes human protein C. Those skilled in the art recognize that the degenerate nature of the genetic code enables one to construct many different DNA sequences that encode the same amino acid residue sequence. The cDNA sequence for nascent human protein C depicted above is thus only one of many possible nascent human protein C-encoding sequences. In constructing the cDNA clones, a 5' poly G sequence, a 3' poly C sequence, and both 5' and 3' PstI restriction enzyme recognition sequences were constructed at the ends of the protein C-encoding cDNA. Two of these cDNA clones were manipulated to construct a DNA molecule comprising both the coding sequence of nascent human protein C and also portions of the DNA encoding the untranslated mRNA at the 5' and 3' ends of the coding region. This DNA molecule was inserted into the PstI site of plasmid pBR322 to construct plasmid pHC7. Plasmid pHC7 thus comprises the coding sequence above and, again depicting only one strand of the molecule, also contains these additional sequences: ##STR2## at the 5' and 3' ends, respectively, of the coding strand of the nascent human protein C coding sequence. Due to the complementary nature of DNA base-pairing, the sequence of one strand of a double-stranded DNA molecule is sufficient to determine the sequence of the opposing strand. Plasmid pHC7 can be conventionally isolated from E. coli K12 RR1/pHC7, a strain deposited with and made part of the permanent stock culture collection of the Northern Regional Research Laboratory (NRRL), Peoria, Ill. A culture of E. coli K12 RRI/pHC7 can be obtained from the NRRL under the accession number NRRL B-15926.

Detailed Description Text (20):

All of the DNA compounds of the present invention were prepared by site-directed mutagenesis of the human protein C gene. The mutagenized zymogen-encoding molecules were then inserted into eukaryotic expression vectors such that expression of the zymogen genes was driven by the major late promoter of adenovirus-2. The vectors also comprise the P2 enhancer element of the BK virus positioned to enhance expression from the promoter. The vectors were transformed into Escherichia coli K12 AG1 cells and deposited and made part of the permanent stock culture collection of the Northern Regional Research Laboratories in Peoria, Ill. 61604. The specific cultures, deposit dates and accession numbers are found in Table II.

Detailed Description Text (22):

To obtain even higher levels of expression, the genes encoding the various zymogen forms of protein C can be cut out of the deposited vectors and ligated into a vector which contains the GBMT transcription control unit. Specifically, plasmid pGTC, which contains the native human protein C gene driven by the GBMT unit, can be obtained (in E. coli K12 AG1) from the NRRL under the accession number NRRL B-18593. The native gene is

removed via digestion of the plasmid grown in a dam.sup.- strain of E. coli with restriction enzyme BclI. The novel zymogen genes can each be removed from their respective plasmids via BclI digestion. The vector backbone is purified and dephosphorylated, then any of the novel zymogen genes of the present invention are ligated into the BclI restriction site. The plasmids comprising the novel zymogen genes positioned for expression behind the GBMT transcription unit are then transformed into 293 cells, cultured and the novel zymogens can be purified from the culture by techniques which are well known in the art. One method for the purification of human protein C from cell culture is disclosed in Yan, U.S. patent application No. 4,981,952, issued Jan. 1, 1991, the entire teaching of which is herein incorporated by reference. The GBMT transcription unit is described in more detail in Grinnell et al., U.S. patent application Ser. No. 07/484,082, filed herewith on even date, the entire teaching of which is herein incorporated by reference.

Detailed Description Text (29):
The vectors of the invention can be transformed into and expressed in a variety of eukaryotic, especially mammalian, host cells. Vectors of the invention that possess no selectable marker with which to isolate and identify stable eukaryotic transformants are useful not only for purposes of transient assay but also for purposes of cotransformation, a procedure disclosed in U.S. Pat. No. 4,399,216, issued Aug. 26, 1983, and incorporated herein by reference. The vectors of the invention can also comprise sequences that allow for replication in E. coli, as it is usually more efficient to prepare plasmid DNA in E. coli than in other host organisms.

Detailed Description Text (57):
Lyophils of E. coli K12 AG1/pLPC-FLIN are obtained from the Northern Regional Research Laboratory, Peoria, Ill. 61604, under the accession number NRRL B-18616. The lyophils are decanted into tubes containing 10 ml LB medium (10 g Bacto-tryptone, 5 g Bacto-yeast extract, and 10 g NaCl per liter; pH is adjusted to 7.5) and incubated two hours at 32.degree. C., at which time the cultures are made 50 .mu.g/ml in ampicillin and then incubated at 37.degree. C. overnight.

Detailed Description Text (58):
A small portion of the overnight culture is placed on LB-agar (LB medium with 15 g/l Bacto-agar) plates containing 50 .mu.g/ml ampicillin in a manner so as to obtain a single colony isolate of E. coli K12 AGl/pLPC-FLIN. The single colony obtained was inoculated into 10 ml of LB medium containing 50 .mu.g/ml ampicillin and incubated overnight at 37.degree. C. with vigorous shaking. The 10 ml overnight culture was inoculated into 500 ml LB medium containing 50 .mu.g/ml ampicillin and incubated at 37.degree. C. with vigorous shaking until the culture reached stationary phase.

Detailed Description Text (68):
Plasmid pGTC is one such vector, wherein the wild type human protein C zymogen gene is driven by the GBMT transcription unit. The wild type protein C gene can be easily removed from the vector on a BclI restriction fragment and any of the genes of the present invention can be inserted into the vector on a BclI restriction fragment. Digestion of plasmid DNA with BclI is inhibited by methylation at adenine in the sequence 5'-GATC-3'. Therefore, plasmid pGTC was prepared from E. coli host cells that lack an adenine methylase, such as that encoded by the dam gene, the product of which methylates the adenine residue in the sequence 5'-GATC-3'. E. coli K12 GM48 (NRRL B-15725) lacks a functional dam methylase and so is a suitable host to use for the purpose of preparing plasmid pGTC DNA for use as starting material in the construction of plasmid derivatives.

Detailed Description Text (69):
E. coli K12 GM48 cells were cultured and made competent for transformation, and plasmid pGTC was used to transform the E. coli K12 GM48 cells in substantial accordance with the procedure of Example 1. The transformed cells were plated on L-agar containing ampicillin, and once the ampicillin-resistant, E. coli K12

GM48/pGTC transformants had formed colonies, one such colony was used to prepare plasmid pGTC DNA in substantial accordance with the procedure of Example 1. About 1 mg of plasmid pGTC DNA was obtained and suspended in about 1 ml of TE buffer. Similarly, plasmids pGT-h and pGT-d can be prepared to allow BclI digestion. Plasmid pGT-d comprises the GBMT transcription unit with no gene at the BclI site, so that any gene can be easily inserted. Plasmid pGT-d also comprises the murine dhfr gene so that any transformant can be selected or amplified using the methotrexate resistance phenotype. Plasmid pGT-h comprises the GBMT transcription unit, a BclI site for easy insertion of a gene of interest and the hygromycin resistance-conferring gene. E. coli K12 AG1 strains comprising each of these plasmids were deposited with the NRRL on Jan. 18, 1990. The strains are available under the accession numbers NRRL B-18591 (for E. coli K12 AG1/pGT-d), NRRL B-18592 (for E. coli K12 AG1/pGT-h), and NRRL B-18593 (for E. coli K12 AG1/pGTC). Restriction site and function maps of these plasmids are presented in the accompanying drawings.

Detailed Description Text (71):
Plasmid pGTC is then isolated from E. coli K12 AG1/pGTC (NRRL B-18593) in substantial accordance with the teaching of Example 1 and prepared from GM48 cells as in Example 2. Plasmid pGTC DNA is then digested with restriction enzyme BclI as taught above, then the large vector fragment is isolated and purified. This vector fragment is brought up to 90 .mu.l volume with TE (pH 8.0), then 10 .mu.l (0.05 Unit) of Calf Instestine Alkaline Phosphatase is added to dephosphorylate the vector ends. The mixture is incubated at 37.degree. C. for 30 minutes, then 10 .mu.l of 500 mM EGTA is added and the reaction is incubated at 65.degree. C. for 45 minutes to inactivate the enzyme. The reaction is then phenol/chloroform extracted, ethanol precipitated, washed and resuspended in 20 .mu.l of water.

Detailed Description Text (73):
Frozen competent E. coli K12 AG1 cells are obtained from Strategene, 3770 Tansey Road, San Diego, Calif. 92121. About 5 .mu.l of the ligation reaction is mixed with a 100 .mu.l aliquot of competent cells, then the cell-DNA mixture is incubated on ice for one hour, heat-shocked at 42.degree. C. for 45 seconds, then chilled on ice for about 2 minutes. The cell-DNA mixture is diluted into 1.0 ml of LB media in a Falcon 2059 tube and incubated at 37.degree. C. for one hour. One hundred microliter aliquots are plated on LB-agar plates containing ampicillin and incubated at 37.degree. C. until colonies appear.

Detailed Description Text (74):
The colonies are individually cultured, and the plasmid DNA of the individual colonies is examined by restriction enzyme analysis. Plasmid DNA isolation is performed on a smaller scale in accordance with the procedure of Example 1, but the CsCl step is omitted until the proper E. coli K12 AG1/pGT-FLIN transformants are identified. At that time, a large scale, highly purified plasmid prep is performed. Following the teaching of Examples 1 and 2, any of the mutant zymogen genes can easily be cloned into any of the GBMT vectors.

Detailed Description Paragraph Table (2):
TABLE II _____ Date Culture Accession Number of Deposit
_____ E. coli K12 AG1/pLPC-N NRRL B-18612 01/09/90 E. coli K12 AG1/pLPC-FN NRRL B-18613 01/09/90 E. coli K12 AG1/pLPC-SC NRRL B-18614 01/13/90 E. coli K12 AG1/pLPC-LIN NRRL B-18615 01/13/90 E. coli K12 AG1/pLPC-FLIN NRRL B-18616 01/13/90

WEST Search History

DATE: Wednesday, August 13, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT; PLUR=YES; OP=AND			
L1	5965415.pn.	1	L1
L2	(dna or deoxy) near3 adenosin$ near3 (methylase or methyltransferase)	3	L2
L3	dam near5 (gene or mutant or mutation or mutagenesis or insertion or substitution or deletion or frameshift)	174	L3
L4	L3 and (coli or salmonell$)	96	L4
L5	$methylase.clm. and (antagonist or antagonize or inhibitors or blocking or blockers or enhancing or enhanced or inactivate or inactivated or modulation or modulator or modulated).clm.	19	L5
L6	(adenine near5 $methylase).clm. and (antagon$ or inhibit$ or block$ or enhanc$ or inactivat$ or modulat$ modulator or reduct$ or decreas$).clm.	0	L6
L7	(adenine near5 $transferase).clm. and (antagon$ or inhibit$ or block$ or enhanc$ or inactivat$ or modulat$ modulator or reduct$ or decreas$).clm.	9	L7
L8	(methyltransferase).clm. and (antagon$ or inhibit$ or block$ or enhanc$ or inactivat$ or modulat$ modulator or reduct$ or decreas$).clm.	58	L8

L9	deoxyadenosine.clm. or deoxy-adenosine.clm. or deoxyadenine.clm. or deoxy-adenine.clm. or (n6 or n-6).clm.	524	L9
L10	deoxyadenosine.clm. or deoxy-adenosine.clm. or deoxyadenine.clm. or deoxy-adenine.clm.	182	L10
L11	l10 and (bacteria$ or microorgan$ or pathogen$ or disease$).clm.	36	L11
L12	(l9 or l10) and gatc.clm.	1	L12

END OF SEARCH HISTORY

WEST

Generate Collection Print

L4: Entry 8 of 96 File: USPT Jun 18, 2002

DOCUMENT-IDENTIFIER: US 6406896 B1
TITLE: Transposase enzyme and method for use

Brief Summary Text (3):
The Tnp protein facilitates movement of the entire element by binding initially to each of two 19 bp specific binding sequences termed outside end (OE; SEQ ID NO:3), followed by formation of a nucleoprotein structure termed a synapse, blunt ended cleavage of each end, association with a target DNA, and then strand transfer (Rezikoff, W. S., Bhasin, A., Davies, D. R., Goryshin, I. Y., Mahnke, L. A., Naumann, T., Rayment, I., Steiniger-White, M., and Twining, S. S., "Tn5: A molecular window on transposition," Biochem. Biophys. Res. Commun. 266:729-34 (1999)). Tn5 transposase can also promote movement of a single ingertion sequence by using a combination of OE and inside end (IE; SEQ ID NO:4) sequences. The IE is also 19 bp long and is identical to OE at 12 of 19 positions (FIG. 1). In vivo, Tn5 transposase exhibits a marked preference for OE in E. coli. Transposase recognition and binding to IE is inhibited in E. coli by the presence of two dam miethylation sites (CATC palindromes) which add four methyl groups per inside end sequence (IE.sup.ME ; also depicted as SEQ ID NO:4, methylation not shown) (Yin, J. C. P., Krebs, M. P., and Reznikoff, W. S., "Effect of dam Methylation on Tn5 Transpositlion," J. Mol Biol., 199:35-45 (1988), incorporated by reference as if set forth herein in its entirety). This methylation reduces transposition by reducing protein-DNA primary recognition (Jilk, R. A., York, D., and Reznikoff, W. S., "The organization of the outside end of transposon Tn5, " J. Bacteriol. 178:1671-1679 (1996)).

Drawing Description Text (5):
FIG. 4 depicts the relative preference of mutant transposases obtained in successive rounds of mutagenesis/recombination for OE and IE in a dam- strain of E. coli.

Detailed Description Text (54):
Mating out assays were performed as described previously (Yin et al., 1988; Goryshin et al., 1994). Bacterial cells with the transposon containing plasmids pFMA52-187 (with either two OEs or two IEs) and the F factor pox-Gen were transformed with the appropriate transposase encoding plasmid pRZ9905. The donor used for the library screening was the strain JCMI0I [.DELTA.(lacZX74, raps, dam-3]. All other mating out was-performed in E. coli strain RZ212 [.DELTA.(lac-proA,B), ara, str, recA56, srl, thi]. The recipient strain used was 14R525[F-na/r]. A total of three assays were performed for each combination of transposase and end sequence, The values reported are the average of these three data points.

Comments

- *FUNCTION*: THIS ENZYME METHYLATES DNA WITHIN THE SEQUENCE GATC. DIRECTLY INVOLVED IN METHYL-DIRECTED DNA MISMATCH REPAIR *(BY SIMILARITY)*.
- *CATALYTIC ACTIVITY*: S-adenosyl-L-methionine + DNA adenine = S-adenosyl-L-homocysteine + DNA 6-methylaminopurine.

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Cross-references

EMBL	U32705; AAC21877.1; [EMBL / GenBank / DDBJ] -. [CoDingSequence]
PIR	H64054; H64054.
HSSP	P04043; 2DPM. [HSSP ENTRY / PDB]
REBASE	1152; M.HindIV.
TIGR	HI0209; -.
InterPro	IPR002294; D12N6_mtfrase. IPR002052; N6_Mtase. Graphical view of domain structure.
Pfam	PF02086; MethyltransfD12; 1.
PRINTS	PR00505; D12N6MTFRASE.
TIGRFAMs	TIGR00571; dam; 1.
PROSITE	PS00092; N6_MTASE; 1.
ProDom	[Domain structure / List of seq. sharing at least 1 domain]
HOBACGEN	[Family / Alignment / Tree]
BLOCKS	P44431.
ProtoNet	P44431.
ProtoMap	P44431.
PRESAGE	P44431.
DIP	P44431.

ModBase	P44431.
SWISS-2DPAGE	Get region on 2D PAGE.

Keywords

Transferase; Methyltransferase; DNA replication; Complete proteome.

Features

None

Sequence information

Length: **286 AA**	Molecular weight: **33218 Da**	CRC64: **BE39C5725AE35DEE** [This is a checksum on the sequence]

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         10          20          30          40          50          60
          |           |           |           |           |           |
MLRPKKQSLK PKLKHRPFLK WAGGKFRLTD EINKAFPNKK NCLIEPFVGA GAVFLNSNFE

         70          80          90         100         110         120
          |           |           |           |           |           |
RYILADINPD LINLFNIVKX NVDGYIEDCK PIFFADDANT PDYYYAKRRQ FNASTEPFER

        130         140         150         160         170         180
          |           |           |           |           |           |
SIIFLYLNRF GFNGLCRYNS KNEFNVPFGA YKTHYFPEDE LRYFAHKAQS AVFLCCDFQK

        190         200         210         220         230         240
          |           |           |           |           |           |
TFEFADKDSV IYCDPPYAPL QQETNFTGYA GNEFGLAQQR ALADLAKSIQ KEKQISILIS

        250         260         270         280
          |           |           |           |
NHDTKFTREI YNGAKFKRVK VQRSISQNPE KRVKVKELIA IFGARK
```

P44431 in FASTA format

View entry in original Swiss-Prot format
View entry in raw text format (no links)
Report form for errors/updates in this Swiss-Prot entry

BLAST — BLAST submission on ExPASy/SIB or at NCBI (USA)

Sequence analysis tools: ProtParam, ProtScale, Compute pI/Mw, PeptideMass, PeptideCutter, Dotlet (Java)

ScanProsite, MotifScan

Search the SWISS-MODEL Repository

The Korean ExPASy site, **kr.expasy.org**, is temporarily not available.

NiceProt View of Swiss-Prot: P44431

Printer-friendly view | Quick BlastP search

Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.

Entry information

Entry name	DMA_HAEIN
Primary accession number	P44431
Secondary accession numbers	None
Entered in Swiss-Prot in	Release 32, November 1995
Sequence was last modified in	Release 32, November 1995
Annotations were last modified in	Release 41, February 2003

Name and origin of the protein

Protein name	**DNA adenine methylase**
Synonyms	**EC 2.1.1.72** **Deoxyadenosyl-methyltransferase** **DNA adenine methyltransferase** **M.HindIV**
Gene name	**DAM** or **HINDIVM** or **HI0209**
From	Haemophilus influenzae [TaxID: 727]
Taxonomy	Bacteria; Proteobacteria; Gammaproteobacteria; Pasteurellales; Pasteurellaceae; Haemophilus.

References

[1] SEQUENCE FROM NUCLEIC ACID.
STRAIN=Rd / KW20 / ATCC 51907;
MEDLINE=95350630; PubMed=7542800; [NCBI, ExPASy, EBI, Israel, Japan]
Fleischmann R.D., Adams M.D., White O., Clayton R.A., Kirkness E.F., Kerlavage A.R., Bult C.J., Tomb J.-F., Dougherty B.A., Merrick J.M., McKenney K., Sutton G., Fitzhugh W., Fields C.A., Gocayne J.D., Scott J.D., Shirley R., Liu L.-I., Glodek A., Kelley J.M., Weidman J.F., Phillips C.A., Spriggs T., Hedblom E., Cotton M.D., Utterback T.R., Hanna M.C., Nguyen D.T., Saudek D.M., Brandon R.C., Fine L.D., Fritchman J.L., Fuhrmann J.L., Geoghagen N.S.M., Gnehm C.L., McDonald L.A., Small K.V., Fraser C.M., Smith H.O., Venter J.C.;
"Whole-genome random sequencing and assembly of Haemophilus influenzae Rd.";
Science 269:496-512(1995).

WEST

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L2: Entry 2 of 3 File: USPT Jun 25, 2002

DOCUMENT-IDENTIFIER: US 6410273 B1
TITLE: Method for producing methylated DNA

Brief Summary Text (34):
After DNA synthesis, some purines and pyrimidines are modified chemically, for example by methylation. Thus, 5-methylcytosine or N.sup.6 -methyladenine participates in the composition of some DNAs. These modifications take place by means of DNA methyltransferases, maintenance or de novo enzymes, which transfer a methyl group from S-adenosyl-L-methionine to adenine or cytosine residues which may be located at specific positions in the sequences. For example, in E. coli, two DNA methyltransferases are well known, the dam DNA methyltransferase which methylates adenosine residues within the sequences 5'-GATC-3', and the dcm DNA methyltransferase which methylates the second cytidine residue of the sequences 5'-CCA/TGG-3'. Other DNA methylases have been studied in bacteria, which methylate a residue contained in a restriction enzyme recognition site. For example, the enzyme M. HpaII methylates the second cytosine residue in the sequence 5'-CCGG-3'.

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QH506 .E5

From: Portner, Ginny
Sent: Wednesday, August 13, 2003 3:05 PM
To: STIC-ILL
Subject: methyltransferase

06825385 91065335 PMID: 2147413
Regulation of pap-pilin phase variation by a mechanism involving differential dam methylation states.
Blyn L B; Braaten B A; Low D A
Department of Pathology, University of Utah School of Medicine, Salt Lake City 84132.
EMBO journal (ENGLAND) Dec 1990, 9 (12) p4045-54, ISSN 0261-4189 Journal Code: 8208664
Contract/Grant No.: 5T32-GM07464; GM; NIGMS; K04-AI00881; AI; NIAID; R01-AI23348; AI; NIAID
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

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(703) 308-7543

STIC-ILL

From: Portner, Ginny
Sent: Wednesday, August 13, 2003 9:57 AM
To: STIC-ILL
Subject: methyltransferase 1645

EQUENCE FROM NUCLEIC ACID.
MEDLINE=83168905; PubMed=6300769; [NCBI, ExPASy, EBI, Israel, Japan]
Brooks J.E., Blumenthal R.M., Gingeras T.R.;
"The isolation and characterization of the Escherichia coli DNA adenine methylase (dam) gene.";
Nucleic Acids Res. 11:837-851(1983).
[2]
SEQUENCE FROM NUCLEIC ACID.
MEDLINE=95327050; PubMed=7603433; [NCBI, ExPASy, EBI, Israel, Japan]
Lyngstadaas A., Lobner-Olesen A., Boye E.;
"Characterization of three genes in the dam-containing operon of Escherichia coli.";
Mol. Gen. Genet. 247:546-554(1995).

SEQUENCE OF 1-18 FROM NUCLEIC ACID.
STRAIN=K12;
MEDLINE=89364696; PubMed=2549371; [NCBI, ExPASy, EBI, Israel, Japan]
Jonczyk P., Hines R., Smith D.W.;
"The Escherichia coli dam gene is expressed as a distal gene of a new operon.";
Mol. Gen. Genet. 217:85-96(1989).
[7]
MUTAGENESIS.
MEDLINE=93341922; PubMed=8341592; [NCBI, ExPASy, EBI, Israel, Japan]
Guyot J.-B., Grassi J., Hahn U., Guschlbauer W.;
"The role of the preserved sequences of Dam methylase.";
Nucleic Acids Res. 21:3183-3190(1993).

SEQUENCE FROM NUCLEIC ACID.
SPECIES=S.typhimurium;
MEDLINE=98241341; PubMed=9575240; [NCBI, ExPASy, EBI, Israel, Japan]
Brawer R., Batista F.D., Burrone O.R., Sordelli D.O., Cerquetti M.C.;
"A temperature-sensitive DNA adenine methyltransferase mutant of Salmonella typhimurium.";
Arch. Microbiol. 169:530-533(1998).
[2]
SEQUENCE FROM NUCLEIC ACID.
SPECIES=S.typhimurium;
STRAIN=LT2 / SGSC1412 / ATCC 700720;
MEDLINE=21534948; PubMed=11677609; [NCBI, ExPASy, EBI, Israel, Japan]
McClelland M., Sanderson K.E., Spieth J., Clifton S.W., Latreille P., Courtney L., Porwollik S., Ali J., Dante M., Du F., Hou S., Layman D., Leonard S., Nguyen C., Scott K., Holmes A., Grewal
N., Mulvaney E., Ryan E., Sun H., Florea L., Miller W., Stoneking T., Nhan M., Waterston R., Wilson R.K.;
"Complete genome sequence of Salmonella enterica serovar Typhimurium LT2.";
Nature 413:852-856(2001).
[3]
SEQUENCE FROM NUCLEIC ACID.
SPECIES=S.typhi;
STRAIN=CT18;
MEDLINE=21534947; PubMed=11677608; [NCBI, ExPASy, EBI, Israel, Japan]
Parkhill J., Dougan G., James K.D., Thomson N.R., Pickard D., Wain J., Churcher C., Mungall K.L., Bentley S.D., Holden M.T.G., Sebaihia M., Baker S., Basham D., Brooks K., Chillingworth T.,
Connerton P., Cronin A., Davis P., Davies R.M., Dowd L., White N., Farrar J., Feltwell T., Hamlin N., Haque A., Hien T.T., Holroyd S., Jagels K., Krogh A., Larsen T.S., Leather S., Moule S.,
O'Gaora P., Parry C., Quail M., Rutherford K., Simmonds M., Skelton J., Stevens K., Whitehead S., Barrell B.G.;
"Complete genome sequence of a multiple drug resistant Salmonella enterica serovar Typhi CT18.";
Nature 413:848-852(2001).

SEQUENCE FROM NUCLEIC ACID.
MEDLINE=94171081; PubMed=8125341; [NCBI, ExPASy, EBI, Israel, Japan]
Bandyopadhyay R., Das J.;
"The DNA adenine methyltransferase-encoding gene (dam) of Vibrio cholerae.";
Gene 140:67-71(1994).
[2]
SEQUENCE FROM NUCLEIC ACID.

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From: Portner, Ginny
Sent: Wednesday, August 13, 2003 9:57 AM
To: STIC-ILL
Subject: methyltransferase 1645

EQUENCE FROM NUCLEIC ACID.
MEDLINE=83168905; PubMed=6300769; [NCBI, ExPASy, EBI, Israel, Japan]
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STRAIN=K12;
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MEDLINE=98241341; PubMed=9575240; [NCBI, ExPASy, EBI, Israel, Japan]
Brawer R., Batista F.D., Burrone O.R., Sordelli D.O., Cerquetti M.C.;
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Gene 140:67-71(1994).
[2]
SEQUENCE FROM NUCLEIC ACID.

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From: Portner, Ginny
Sent: Wednesday, August 13, 2003 3:08 PM
To: STIC-ILL
Subject: methyltransferase

05847989 88201988 PMID: 3283540
Frameshift lesions induced by oxazolopyridocarbazoles are recognized by the mismatch repair system in Escherichia coli.
Rene B; Auclair C; Paoletti C
Laboratoire de Biochimie-Enzymologie, INSERM U140, CNRS UA147, Institut Gustave Roussy, Villejuif, France.
Mutation research (NETHERLANDS) May 1988, 193 (3) p269-73, ISSN 0027-5107 Journal Code: 0400763
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

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From: Portner, Ginny
Sent: Wednesday, August 13, 2003 9:57 AM
To: STIC-ILL
Subject: methyltransferase 1645

EQUENCE FROM NUCLEIC ACID.
MEDLINE=83168905; PubMed=6300769; [NCBI, ExPASy, EBI, Israel, Japan]
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Mol. Gen. Genet. 247:546-554(1995).

duplicate

SEQUENCE OF 1-18 FROM NUCLEIC ACID.
STRAIN=K12;
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Jonczyk P., Hines R., Smith D.W.;
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N., Mulvaney E., Ryan E., Sun H., Florea L., Miller W., Stoneking T., Nhan M., Waterston R., Wilson R.K.;
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Gene 140:67-71(1994).
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SEQUENCE FROM NUCLEIC ACID.

STIC-ILL

From: Portner, Ginny
Sent: Wednesday, August 13, 2003 8:27 AM
To: STIC-ILL
Subject: methyltransferase

Brooks, J. E., Blumenthal, R. M., and Gingeras, T. R., (1993). The isolation and characterization of the Escherichia coli DNA adenine methylase (DAM) gene. Nucl Acids Res. 11:837-851.

Brooks et al. "The isolation and Characterization of the Escherichia coli DNA Adenine Methylasse (dam) Gene," Nucl. Acids Res. 1(3):837-51 (1983).

(The citations were found in a patent; one of them appears to be in error, but I am not sure which one it is)

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QP620.N8
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STIC-ILL

From: Portner, Ginny
Sent: Wednesday, August 13, 2003 9:57 AM
To: STIC-ILL
Subject: methyltransferase 1645

EQUENCE FROM NUCLEIC ACID.
MEDLINE=83168905; PubMed=6300769; [NCBI, ExPASy, EBI, Israel, Japan]
Brooks J.E., Blumenthal R.M., Gingeras T.R.;
"The isolation and characterization of the Escherichia coli DNA adenine methylase (dam) gene.";
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SEQUENCE OF 1-18 FROM NUCLEIC ACID.
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"Complete genome sequence of Salmonella enterica serovar Typhimurium LT2.";
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Bandyopadhyay R., Das J.;
"The DNA adenine methyltransferase-encoding gene (dam) of Vibrio cholerae.";
Gene 140:67-71(1994).
[2]
SEQUENCE FROM NUCLEIC ACID.

MIC
QR1 J8

STIC-ILL

From: Portner, Ginny
Sent: Wednesday, August 13, 2003 3:06 PM
To: STIC-ILL
Subject: methyltransferase

06545677 90170830 PMID: 2155196
Specific A/G-to-C.G mismatch repair in Salmonella typhimurium LT2 requires the mutB gene product.
Lu A L; Cuipa M J; Ip M S; Shanabruch W G
Department of Biological Chemistry, School of Medicine, University of Maryland, Baltimore 21201.
Journal of bacteriology (UNITED STATES) Mar 1990, 172 (3) p1232-40, ISSN 0021-9193 Journal Code: 2985120R
Contract/Grant No.: BRSG 11; RS; DRS; GM35132; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

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MIC
QR1 J8

STIC-ILL

From: Portner, Ginny
Sent: Wednesday, August 13, 2003 3:07 PM
To: STIC-ILL
Subject: methyltransferase

06384373 90008766 PMID: 2676972
Nucleotide sequence of the Salmonella typhimurium mutL gene required for mismatch repair: homology of MutL to HexB of Streptococcus pneumoniae and to PMS1 of the yeast Saccharomyces cerevisiae.
Mankovich J A; McIntyre C A; Walker G C
Department of Biology, Massachusetts Institute of Technology, Cambridge 02139.
Journal of bacteriology (UNITED STATES) Oct 1989, 171 (10) p5325-31, ISSN 0021-9193 Journal Code: 2985120R
Contract/Grant No.: GM10792; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
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MIC
QH426.M6

STIC-ILL

From: Portner, Ginny
Sent: Wednesday, August 13, 2003 8:49 AM
To: STIC-ILL
Subject: methyltransferase

Importance: High

Marinus et al., Mol. Gen. Genet., 192, pp. 288-289 (1983) "Insertion Mutations in the dam gene of Escherichia coli K-12".

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(703) 308-7543

MIC

QR1.J8

STIC-ILL

From: Portner, Ginny
Sent: Wednesday, August 13, 2003 3:08 PM
To: STIC-ILL
Subject: methyltransferase

05249481 86250633 PMID: 3522556
Mutant of Salmonella typhimurium LT2 deficient in DNA adenine methylation.
Ritchie L J; Hall R M; Podger D M
Journal of bacteriology (UNITED STATES) Jul 1986, 167 (1) p420-2, ISSN 0021-9193 Journal Code: 2985120R
Document type: Journal Article
Languages: ENGLISH
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STIC-ILL MPL

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EQUENCE FROM NUCLEIC ACID.
MEDLINE=83168905; PubMed=6300769; [NCBI, ExPASy, EBI, Israel, Japan]
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SPECIES=S.typhimurium;
STRAIN=LT2 / SGSC1412 / ATCC 700720;
MEDLINE=21534948; PubMed=11677609; [NCBI, ExPASy, EBI, Israel, Japan]
McClelland M., Sanderson K.E., Spieth J., Clifton S.W., Latreille P., Courtney L., Porwollik S., Ali J., Dante M., Du F., Hou S., Layman D., Leonard S., Nguyen C., Scott K., Holmes A., Grewal
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01809394  ORDER NO: AADAA-I9937656
 Regulation of Salmonella  typhimurium plasmid-encoded  fimbriae
  Author:  Nicholson, Bradly Paul
  Degree:  Ph.D.
  Year:    1999
  Corporate Source/Institution:  The University of Utah (0240)
  Adviser: David A. Low
  Source:  VOLUME 60/07-B OF DISSERTATION ABSTRACTS INTERNATIONAL.
           PAGE 3091.  121 PAGES
  Descriptors:  BIOLOGY, GENETICS ; BIOLOGY, MOLECULAR ; BIOLOGY,
                MICROBIOLOGY
  Descriptor Codes:  0369; 0307; 0410
  ISBN:         0-599-38929-X
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Bacteria interact with their environment through proteinacious fibers known as fimbriae. Fimbrial expression is regulated in response to environmental stimuli. Some fimbriae undergo phase variation, which results in a population of bacteria skewed between fimbrial expression (phase ON) and non-expression (phase OFF) under inducing conditions. Transcriptional phase variation can be regulated by methylation of GATC DNA sequences, which are targets of DNA adenine methylase (Dam). This dissertation investigates the regulation and phase variation of <italic>Salmonella typhimurium</italic> plasmid encoded fimbriae (<italic>pef</italic>). The Pef operon shares features with the <italic> E. coli</italic> pyleonephritis associated pilus (<italic>pap</italic>) operon, which is regulated by a methylation dependent transcriptional switch. Expression of Pef fimbriae was induced in standing culture at low pH (pH 5.1). Transcription of <italic>pef</italic> was dependent on Leucine responsive regulatory protein (Lrp) and DNA adenine methylase (Dam). Lrp was essential for methylation protection of the <italic>pef</italic> GATC sites. Based on genetic analyses, methylation of GATC II was necessary for activation of

<italic>pef</italic> transcription. Expression of the <italic>pef</italic> operon was inhibited by the histone like protein (H-NS) and the stationary phase sigma factor (RpoS). The <italic> pef</italic> operon is the first example of methylation dependent fimbrial regulation outside of <italic>E. coli.</italic>

3/9/2

01501116 ORDER NO: AAD96-27127
THE MOLECULAR BASIS **OF PYELONEPHRITIS-ASSOCIATED** PILI PHASE **VARIATION IN ESCHERICHIA** COLI

Author: NOU, XIANGWU
Degree: PH.D.
Year: 1996
Corporate Source/Institution: THE UNIVERSITY OF UTAH (0240)
Source: VOLUME 57/04-B OF DISSERTATION ABSTRACTS INTERNATIONAL.
PAGE 2362. 128 PAGES
Descriptors: BIOLOGY, MOLECULAR ; BIOLOGY, MICROBIOLOGY ; BIOLOGY, GENETICS
Descriptor Codes: 0307; 0410; 0369

The expression of pyelonephritis-associated pili (Pap) in Escherichia coli is under a phase variation control mechanism in which individual cells alternate between pili$\sp{+}$ (ON) and pili$\sp{-}$ (OFF) states. This occurs through a process involving DNA methylation by deoxyadenosine methylase (Dam). Methylation of two GATC sites (GATC-I and GATC-II) within the pap regulatory region is differentially inhibited in phase ON and phase OFF cells. The GATC-I site of phase ON cells is nonmethylated and GATC-II site is fully methylated. Conversely, in phase OFF cells the GATC-I site is fully methylated whereas the GATC-II site is nonmethylated. Two transcription activators, Lrp and PapI, are required for this specific methylation inhibition. Low resolution DNA footprint analyses using nonmethylated pap DNA indicated that Lrp binds near the GATC-II, whereas PapI does not bind specifically to pap regulatory region. However, the addition of Lrp and PapI together resulted in an additional footprint around the GATC-I site, indicating that both Lrp and PapI are required for binding to the GATC-I region.

To define the role of Dam methylation in pap gene regulation, the GATC-I and GATC-II sites were mutated so that they could not be methylated, and the effects of these mutations on Pap phase variation were examined. The results indicated that methylation of GATC-I blocks formation of the phase ON state by inhibiting PapI-dependent Lrp binding to this DNA region. In contrast, methylation of GATC-II is required for the phase OFF to ON transition. Evidence suggests that this occurs by the inhibition of Lrp to sites overlapping the papBA promoter, which may occlude RNA polymerase.

The Lrp binding sites in the pap regulatory region were further defined by methylation protection analysis. Six Lrp binding sites were found, each separated by about three helical turns of DNA. Lrp bound with highest affinity to three sites (1, 2, and 3) proximal to the papBA promoter. A mutational analysis indicated that the binding of Lrp to sites 2 and 3 inhibits pap transcription, which is consistent with the fact that Lrp binding site 3 is located between the $-$35 and $-$10 RNA polymerase binding region of papBA promoter. The addition of PapI decreased the affinity of Lrp for sites 1, 2, and 3 and increased its affinity for the distal Lrp binding sites 4 and 5. Mutations within Lrp binding sites 4 and 5 shut off pap transcription, indicating that the binding of Lrp to this pap region activated transcription. The pap GATC-I and GATC-II sites are located within Lrp binding sites 5 and 2, respectively, providing a mechanism by which Dam controls Lrp binding and Pap phase variation. A model for Pap phase variation is presented based on these results.

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00509816 (USE 9 FOR FULLTEXT)

An Essential Role for DNA Adenine Methylation in Bacterial Virulence

Heithoff, Douglas M.; Sinsheimer, Robert L.; Low, David A.; Mahan, Michael J.<CRF RID="C1">
Department of Molecular, Cellular, and Developmental Biology, University of California, Santa Barbara, CA 93106, USA.

Science Vol. 284 5416 pp. 967
Publication Date: 5-07-1999 (990507) Publication Year: 1999
Document Type: Journal ISSN: 0036-8075
Language: English
Section Heading: REPORTS
Word Count: 2380

(THIS IS THE FULLTEXT)

...Abstract: Dam methylation at specific genomic sites, as evidenced by alterations in DNA methylation patterns. Dam **inhibitors** are likely to have broad **antimicrobial** action, and Dam.sup(-) derivatives of these pathogens may serve as live attenuated vaccines

...Text: latter regulatory mechanism involves formation of heritable DNA methylation patterns, which control gene expression by **modulating** the binding of regulatory proteins. Although Dam regulates pili gene expression, its role in microbial...

...Dam controls the expression of Pap pili by **modulating** the binding of leucine-responsive regulatory protein (Lrp) to pap regulatory DNA sequences (B3) . Lrp...

...to facilitate growth at systemic sites of infection (B12) ; pmrB is involved in resistance to **antibacterial** peptides termed ...2 to 19 (Fig. 2), and this repression was not dependent on the PhoP protein. **Dam** did not significantly affect the expression of the remaining four PhoP-activated genes (B17) . These...

...regulatory proteins to DNA can form DNA methylation patterns by blocking the methylation of specific **Dam** target sites (**GATC** sequences) (B18) . Therefore, we further investigated the interactions between **Dam** and PhoP by determining whether the binding of PhoP (or a PhoP-regulated protein) to specific DNA sites blocks methylation of these sites by **Dam** , resulting in an alteration in the DNA methylation pattern. Analysis of PhoP.sup(+) and PhoP...
...of genomic DNA from PhoP.sup(-) bacteria with Mbo I (which cleaves only at nonmethylated **GATC** sites) resulted in the appearance of DNA fragments that were not present in DNA from PhoP.sup(+) bacteria, indicating that the PhoP protein (or a PhoP-regulated gene product) blocks **Dam** methylation at specific **GATC** -containing sites in the Salmonella genome (Fig. 3, arrows). Recent data have shown that although catabolite gene activator protein binds to a DNA sequence containing **GATC** , it does not protect this site from methylation (B18) . Thus, not every protein that binds to a **Dam** target site protects the **GATC** sequence from methylation. It is also possible that PhoP.sup(+) and PhoP.sup(-) strains have different amounts of **Dam** activity, which in turn could affect DNA methylation patterns. However, this regulation does not occur at the transcriptional level because **Dam** does not alter PhoP expression, nor does PhoP alter **Dam** expression (B17) . Further analysis will determine whether these PhoP-protected sites are within regulatory regions...

...In E. coli, almost all **GATC** sites protected from methylation are in 5 (prime) noncoding DNA regions presumably involved in the...

...patterns identified in Salmonella (Fig. 3) are also within gene regulatory regions. Methylation of specific **GATC** sites in the regulatory regions of virulence genes could affect the binding of regulatory proteins ...

...as has been shown for the pap virulence operon in E. coli (B7) (B18) . Similarly, **Dam** methylation could directly or indirectly affect the expression of PhoPQ-regulated genes in S. typhimurium...DNA adenine

methylases are potentially excellent targets for both vaccines and **antimicrobials** . They are highly conserved in many pathogenic bacteria that cause significant morbidity and mortality, such...

...that share common epitopes. Finally, because the Dam methylase is essential for bacterial virulence, Dam **inhibitors** are likely to have broad **antimicrobial** action, hence Dam is a promising target for **antimicrobial** drug development...

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Set	Items	Description

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	47679	SALMONEL?
	4020	DAM
S1	36	SALMONEL? (100N) DAM

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06545677 90170830 PMID: 2155196

Specific A/G-to-C.G mismatch repair in Salmonella typhimurium LT2 requires the mutB gene product.

Lu A L; Cuipa M J; Ip M S; Shanabruch W G

Department of Biological Chemistry, School of Medicine, University of Maryland, Baltimore 21201.

Journal of bacteriology (UNITED STATES) Mar 1990, 172 (3) p1232-40, ISSN 0021-9193 Journal Code: 2985120R

Contract/Grant No.: BRSG 11; RS; DRS; GM35132; GM; NIGMS

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

An assay has been developed that permits analysis of repair of A/G mismatches to C.G base pairs in cell extracts of **Salmonella** typhimurium LT2. This A/G mismatch repair is independent of ATP, **dam** methylation, and mutS gene function. The gene product of mutB has been shown to be involved in the **dam** -independent pathway through the in vitro assay. Moreover, specific DNA-protein complexes and an endonuclease can be detected in S. typhimurium extracts by using DNA fragments containing an A/G mismatch. These activities are not observed with substrates which have a T/G mismatch or no mismatch. The S. typhimurium endonuclease, like the A/G endonuclease found in Escherichia coli (A-L. Lu and D.-Y. Chang, Cell 54:805-812, 1988), makes incisions at the first phosphodiester bond 3' to and the the second phosphodiester bond 5' to the dA of the A/G mismatch. No incision site was detected on the other DNA strand. Extracts prepared from mutB mutants cannot form A/G mismatch-specific DNA-protein complexes and do not contain the A/G endonuclease activity. Thus the A/G mismatch specific binding and nicking activities are probably involved in the A/G mismatch repair pathway. Preliminary analysis of the mutational spectrum of the mutB strain has indicated that this mutator allele causes an increase in C.G-to-A.T transversions without affecting the frequencies of other transversion or transition events. In addition, the mutB gene has been mapped to the 64-min region of the S. typhimurium chromosome. Together, this biochemical and genetic evidence suggests that the mutB gene product of S. typhimurium is the homolog of the E. coli micA (and/or mutY) gene product.

Tags: Support, U.S. Gov't, P.H.S.

Descriptors: *Adenine; *Bacterial Proteins--genetics--GE; *Base Composition; *Cytosine; *DNA Repair; *Guanine; *Mutation; *N-glycosyl Hydrolases--genetics--GE; *Salmonella typhimurium--genetics--GE; Bacterial Proteins--metabolism--ME; Base Sequence; DNA Transposable Elements; DNA-Binding Proteins--metabolism--ME; Escherichia coli--genetics--GE; Genotype; Molecular Sequence Data; N-glycosyl Hydrolases--metabolism--ME; Oligonucleotide Probes; Transduction, Genetic

CAS Registry No.: 0 (Bacterial Proteins); 0 (DNA Transposable Elements); 0 (DNA-Binding Proteins); 0 (Oligonucleotide Probes); 71-30-7 (Cytosine); 73-24-5 (Adenine); 73-40-5 (Guanine)

Enzyme No.: EC 3.2.2.- (N-glycosyl Hydrolases)

Record Date Created: 19900411

Record Date Completed: 19900411

05964198 88318765 PMID: 2842672

A mutation in the DNA adenine methylase gene (dam) of Salmonella typhimurium decreases susceptibility to 9-aminoacridine-induced frameshift mutagenesis.

Ritchie L; Podger D M; Hall R M
CSIRO Division of Molecular Biology, North Ryde, NSW, Australia.

Mutation research (NETHERLANDS) Sep 1988, 194 (2) p131-41, ISSN 0027-5107 Journal Code: 0400763
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

A mutant of **Salmonella** typhimurium with a reduced response to mutation induction by 9-aminoacridine (9AA) has been isolated. The mutation (**dam** -2) is located in the DNA adenine methylase gene. The **dam** -2 mutant strain exhibits a level of sensitivity to 2-aminopurine (2AP) intermediate between that of the **dam** + and the DNA adenine methylation-deficit **dam** -1 strain, and 2AP sensitivity was reversed by introduction of a mutH mutation or of the plasmid pMQ148 (which carries a functional Escherichia coli **dam** + gene). However, the **dam** -2 strain is not grossly defective in DNA adenine methylase activity. Whole cell DNA appears full methylated at -GATC- sites. The levels of 9AA required to induce equivalent levels of frameshift mutagenesis in the dam-2 strain were approximately 2-fold higher than for the dam+ strain. Introduction of pMQ148 dam+ reduced the level of 9AA required for induction of frameshift mutations 4-fold in the dam-2 strain and 2-fold in the dam+ strain. The dam-2 mutation had no effect on the levels of ICR191 required for induction of frameshift mutations, but introduction of pMQ148 reduced the ICR191-induced mutagenesis 2-fold. The dam+/pMQ148, dam-2/pMQ148 and dam-1/pMQ148 strains showed identical dose-response curves for both 9AA and ICR191. These results are consistent with a slightly reduced (dam-2) or increased (pMQ148) rate of methylation at the replication fork. The 2AP sensitivity of the dam-2 strain cannot be simply explained. Furthermore, addition of methionine to the assay medium reverses the 2AP sensitivity of the dam-2 strain, but has no effect on 9AA mutagenesis.

Descriptors: *Aminacrine--pharmacology--PD; *Aminoacridines--pharmacology --PD; *Genes, Bacterial; *Genes, Structural; *Methyltransferases--genetics --GE; *Mutation; *Salmonella typhimurium--genetics--GE; DNA Transposable Elements; Genotype; Microbial Sensitivity Tests; Salmonella typhimurium --drug effects--DE; Salmonella typhimurium--enzymology--EN; Site-Specific DNA-Methyltransferase (Adenine-Specific); Species Specificity
CAS Registry No.: 0 (Aminoacridines); 0 (DNA Transposable Elements); 90-45-9 (Aminacrine)
Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific))
Record Date Created: 19881004
Record Date Completed: 19881004

05249481 86250633 PMID: 3522556

Mutant of Salmonella typhimurium LT2 deficient in DNA adenine methylation.

Ritchie L J; Hall R M; Podger D M

Journal of bacteriology (UNITED STATES) Jul 1986, 167 (1) p420-2, ISSN 0021-9193 Journal Code: 2985120R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

A mutant of **Salmonella** typhimurium LT2 deficient in methylation of the adenine residues in the sequence 5'-GATC-3' was isolated. The mutation (**dam** -1) was linked to the cysG locus, and the properties of the mutant were similar to those of Escherichia coli **dam** mutants. Reversion of the hisC3076 frameshift marker by 9-aminoacridine was substantially enhanced by the **dam** -1 mutation, implying a direct role for adenine methylation in the prevention of frameshift mutation induction.

Descriptors: *Adenine--metabolism--ME; *DNA, Bacterial--metabolism--ME; *Mutation; *Salmonella typhimurium--genetics--GE; Aminacrine--pharmacology --PD; Genes, Bacterial; Methylation; Methyltransferases--genetics--GE; Methyltransferases--metabolism--ME; Salmonella typhimurium--metabolism--ME ; Site-Specific DNA-Methyltransferase (Adenine-Specific)

CAS Registry No.: 0 (DNA, Bacterial); 73-24-5 (Adenine); 90-45-9 (Aminacrine)

Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific))

Record Date Created: 19860811

Record Date Completed: 19860811

10662852 97011573 PMID: 8858583

The clp (CS31A) operon is negatively controlled by Lrp, ClpB, and L-alanine at the transcriptional level.

Martin C

Laboratoire de Microbiologie, Institut National de la Recherche Agronomique, Saint-Genes-Champanelie, France. cmartin@clermont.inra.fr

Molecular microbiology (ENGLAND) Jul 1996, 21 (2) p281-92, ISSN 0950-382X Journal Code: 8712028

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Biosynthesis of the Escherichia coli CS31A surface antigen was subject to phase-variation control and repressed by L-alanine. Nucleotide sequence analysis of the clp operon, encoding the biosynthesis of CS31A, revealed the presence of a regulatory gene, clpB. The amino acid sequence of the regulatory protein ClpB showed similarity to the primary structure of PapB, FaeB and AfaA, involved in the regulation of expression of Pap, K88, and Afa-3 fimbriae, respectively. The clp regulatory region contained two deoxyadenosine methylase sites (**GATC** -I and **GATC** -II). The leucine-responsive regulatory protein (Lrp) was required for specific methylation **inhibition** of the **GATC** -II site. The activity of the clp promoter was monitored in a clp-lacZYA single-copy fusion. The cloned DNA used in this study did not contain a related papI gene. In these conditions, we showed, as expected, that phase variation did not occur. However, transcription of the clp operon was negatively controlled by ClpB and Lrp, and was maximal in the absence of **Dam** methylase. In the presence of AfaF, a PapI equivalent, the phase-variation control was restored. We concluded that two regulatory mechanisms were superimposed to control the clp expression. Phase variation, mediated by Lrp and a PapI equivalent, controlled the number of cells producing CS31A in a single colony. The second mechanism, described in this report, was mediated by ClpB and Lrp and controls the level of CS31A produced by a single cell. Furthermore, we showed that L-alanine reduced, by about twofold, the clp promoter activity independently of a PapI equivalent, ClpB, Lrp or Dam methylase. In addition, the presence of L-alanine prevented the phase-variation control mediated by AfaF.

Tags: Comparative Study

10604562 96422150 PMID: 8824767

Importance of the replication origin sequestration in cell division of Escherichia coli.

Meury J; Bahloul A; Kohiyama M
Biochimie Genetique, Universite Paris, France.

Biochimie (FRANCE) 1995, 77 (11) p875-9, ISSN 0300-9084
Journal Code: 1264604
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

The DNA adenine **methyltransferase** of Escherichia coli methylates adenines at **GATC** sequences. The mutant deficient in this methylase has no apparent deficiency in the cell division process in spite of the absence of both synchrony in initiations of chromosomal DNA replication and sequestration of replication origin (oriC) at hemimethylated state. However, the **dam** mutant cannot resume cell division after hyperosmotic shock differing from the wild-type strain. This **inhibition** is not provoked by induction of the cell division **inhibitor** , SfiA protein. Although the FtsZ protein is present in the **dam** mutant in a reduced amount compared to wild-type, the quantitative difference of this protein is not the main reason of division arrest provoked by hyperosmotic shock. This observation supports the idea of oriC-membrane interaction playing a role both in chromosome partitioning and cell division as predicted by replicon theory.

Tags: Support, Non-U.S. Gov't
Descriptors: *Bacterial Proteins--metabolism--ME; *DNA, Bacterial --genetics--GE; *Escherichia coli--genetics--GE; *Escherichia coli--growth and development--GD; *Replication Origin--physiology--PH; Bacterial Proteins--genetics--GE; Betaine--pharmacology--PD; Cell Division; Mutation
CAS Registry No.: 0 (Bacterial Proteins); 0 (DNA, Bacterial); 0 (FtsZ protein); 0 (sulA protein, E coli); 107-43-7 (Betaine)
Record Date Created: 19961205
Record Date Completed: 19961205

10310697 96112794 PMID: 8846772

Differential binding of Lrp to two sets of pap DNA binding sites mediated by Pap I regulates Pap phase variation in Escherichia coli.

Nou X; Braaten B; Kaltenbach L; Low D A

Department of Pathology, University of Utah, Salt Lake City 84132, USA.

EMBO journal (ENGLAND) Dec 1 1995, 14 (23) p5785-97, ISSN 0261-4189 Journal Code: 8208664

Contract/Grant No.: 2R01 AI23348; AI; NIAID

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Pyelonephritis-associated pili (Pap) expression in Escherichia coli is subject to a phase variation control mechanism that is regulated by the leucine-responsive regulatory protein (Lrp), PapI, and deoxyadenosine methylase (**Dam**). In previous work, we found that the differential **Dam** methylation of two target sites in pap regulatory DNA, **GATC** -I and **GATC** II, is essential for the transition between active and inactive pap transcriptional states. Here, we identify six Lrp binding sites within the pap regulatory DNA, each separated by about three helical turns. Lrp binds with highest affinity to three sites (1, 2 and 3) proximal to the papBAp promoter. A mutational analysis indicates that the binding of Lrp to sites 2 and 3 **inhibits** pap transcription, which is consistent with the fact that Lrp binding site 3 is located between the --35 and --10 RNA polymerase binding region of papBAp. The addition of PapI decreases the affinity of Lrp for sites 1, 2 and 3 and increases its affinity for the distal Lrp binding sites 4 and 5. Mutations within Lrp binding sites 4 and 5 shut off pap transcription, indicating that the binding of Lrp to this pap region activates pap transcription. The pap **GATC** -I and **GATC** -II methylation sites are located within Lrp binding sites 5 and 2, respectively, providing a mechanism by which **Dam** controls Lrp binding and Pap phase variation.

Tags: Support, U.S. Gov't, P.H.S.

Descriptors: *Bacterial Proteins--metabolism--ME; *DNA, Bacterial --metabolism--ME; *DNA-Binding Proteins--metabolism--ME; *Escherichia coli --genetics--GE; *Fimbriae, Bacterial--genetics--GE; *Transcription Factors --metabolism--ME; Bacterial Proteins--genetics--GE; Base Sequence; Binding Sites; DNA Footprinting; DNA, Bacterial--genetics--GE; DNA-Binding Proteins --genetics--GE; Escherichia coli--ultrastructure--UL; Gene Expression Regulation, Bacterial--genetics--GE; Methylation; Models, Genetic; Molecular Sequence Data; Mutagenesis, Site-Directed--genetics--GE; Nucleic Acid Conformation; Phenotype; Site-Specific DNA-Methyltransferase (Adenine-Specific)--metabolism--ME; Transcription Factors--genetics--GE; Transcription, Genetic--genetics--GE

CAS Registry No.: 0 (Bacterial Proteins); 0 (DNA, Bacterial); 0 (DNA-Binding Proteins); 0 (PapI protein); 0 (Transcription Factors); 138791-20-5 (leucine-responsive regulatory protein)

Enzyme No.: EC 2.1.1.- (Dam methyltransferase); EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific))

Record Date Created: 19961021

07427672 92291095 PMID: 1601880

Initiation of methyl-directed mismatch repair.

Au K G; Welsh K; Modrich P

Department of Biochemistry, Duke University Medical Center, Durham, North Carolina 27710.

Journal of biological chemistry (UNITED STATES) Jun 15 1992, 267 (17) p12142-8, ISSN 0021-9258 Journal Code: 2985121R

Contract/Grant No.: GM23719; GM; NIGMS

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Escherichia coli MutH possesses an extremely weak d(GATC) endonuclease that responds to the state of methylation of the sequence (Welsh, K. M., Lu, A.-L., Clark, S., and Modrich, P. (1987) J. Biol. Chem. 262, 15624-15629). MutH endonuclease is activated in a reaction that requires MutS, MutL, ATP, and Mg2+ and depends upon the presence of a mismatch within the DNA. The degree of activation correlates with the efficiency with which a particular mismatch is subject to methyl-directed repair (G-T greater than G-G greater than A-C greater than C-C), and activated MutH responds to the state of DNA adenine methylation. Incision of an unmethylated strand occurs immediately 5' to a d(**GATC**) sequence, leaving 5' phosphate and 3' hydroxy termini (pN decreases pGpAp-TpC). Unmethylated d(**GATC**) sites are subject to double strand cleavage by activated MutH, an effect that may account for the killing of **dam** - mutants by 2-aminopurine. The mechanism of activation apparently requires ATP hydrolysis since adenosine-5'-O-(3-thiotriphosphate) not only fails to support the reaction but also **inhibits** activation promoted by ATP. The process has no obligate polarity as d(**GATC**) site incision by the activated nuclease can occur either 3' or 5' to the mismatch on an unmethylated strand. However, activation is sensitive to DNA topology. Circular heteroduplexes are better substrates than linear molecules, and activity of DNAs of the latter class depends on placement of the mismatch and d(**GATC**) site within the molecule. MutH activation is supported by a 6-kilobase linear heteroduplex in which the mismatch and d(GATC) site are centrally located and separated by 1 kilobase, but a related molecule, in which the two sites are located near opposite ends of the DNA, is essentially inactive as substrate. We conclude that MutH activation represents the initiation stage of methyl-directed repair and suggest that interaction of a mismatch and a d(GATC) site is provoked by MutS binding to a mispair, with subsequent ATP-dependent translocation of one or more Mut proteins along the helix leading to cleavage at a d(GATC) sequence on either side of the mismatch.

Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Descriptors: *DNA Repair; *Escherichia coli--genetics--GE; *Nucleic Acid Heteroduplexes; Adenosine Triphosphate--analogs and derivatives--AA; Adenosine Triphosphate--metabolism--ME; Bacterial Proteins--metabolism--ME; Base Sequence; Cations, Divalent; DNA, Bacterial--genetics--GE; DNA, Bacterial--metabolism--ME; DNA-Binding Proteins--metabolism--ME; Electrophoresis, Polyacrylamide Gel; Endodeoxyribonucleases--metabolism--ME; Genes, Bacterial; Hydrolysis; Magnesium--metabolism--ME; Methylation; Molecular Sequence Data; Nucleic Acid Conformation; Substrate Specificity

CAS Registry No.: 0 (Bacterial Proteins); 0 (Cations, Divalent); 0 (DNA, Bacterial); 0 (DNA-Binding Proteins); 0 (MutS protein); 0 (Nucleic Acid Heteroduplexes); 35094-46-3 (adenosine 5'-O-(3-thiotriphosphate)); 56-65-5 (Adenosine Triphosphate); 7439-95-4 (Magnesium)

Enzyme No.: EC 3.1.- (Endodeoxyribonucleases); EC 3.1.21.- (MutH gene product)

Record Date Created: 19920716

Record Date Completed: 19920716

07371801 92234969 PMID: 1569034

Escherichia coli cells lacking methylation- blocking **factor (leucine-responsive regulatory protein) have precise timing of initiation of DNA replication in the cell cycle.**

Smith D W; Stine W B; Svitil A L; Bakker A; Zyskind J W

Department of Biology, University of California, San Diego, La Jolla 92093.

Journal of bacteriology (UNITED STATES) May 1992, 174 (9) p3078-82, ISSN 0021-9193 Journal Code: 2985120R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

A protein that is required for specific methylation **inhibition** of two **GATC** sites in the papBA pilin promoter region, known as methylation-**blocking** factor (Mbf) and recently shown to be identical to the leucine-responsive regulatory protein (Lrp), is not responsible for the delayed methylation at oriC implicated in an eclipse period following initiation of DNA replication. Cells containing a transposon mutation within the mbf (lrp) gene initiate DNA replication at the correct time during the cell cycle, whereas cells with increased amounts of the **Dam methyltransferase** initiate DNA replication randomly throughout the cell cycle.

Tags: Support, U.S. Gov't, Non-P.H.S.

Descriptors: *Bacterial Proteins--genetics--GE; *Cell Cycle--genetics--GE ; *DNA Replication--genetics--GE; *DNA-Binding Proteins--genetics--GE; *Escherichia coli--genetics--GE; Gene Expression Regulation, Bacterial; Methyltransferases--biosynthesis--BI; Mutation; Time Factors

CAS Registry No.: 0 (Bacterial Proteins); 0 (DNA-Binding Proteins); 138791-20-5 (leucine-responsive regulatory protein)

Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.- (Dam methyltransferase)

Record Date Created: 19920522

Record Date Completed: 19920522

in their recognition sequence failed to cut pCSL17 from C. glutamicum, whereas enzymes which require methylation at adenosine in **GATC** sequences failed to cut. Failure of HaeIII to cut two specific sites of C. glutamicum-derived pCSL17 identified the first cytidine in the sequence GGCCGC as one target of methylation in this species, which contains the **methyltransferase** recognition sequence. Although Brevibacterium lactofermentum-derived DNA showed a similar methylation pattern by HPLC analysis, HaeIII cleaved these GGCCGC sites, suggesting differences in the specificity of methylation between these two species. Results for all analyses of B. flavum DNA were identical to those for C. glutamicum.

Descriptors: *Corynebacterium--genetics--GE; *Nucleotides--metabolism--ME ; Base Sequence; DNA, Bacterial--analysis--AN; Escherichia coli--genetics --GE; Methylation; Methyltransferases--metabolism--ME; Plasmids--genetics --GE; Restriction Mapping; Sequence Analysis, DNA

CAS Registry No.: 0 (DNA, Bacterial); 0 (Nucleotides); 0 (Plasmids)

Enzyme No.: EC 2.1.1. (Methyltransferases)

Record Date Created: 19961118

Record Date Completed: 19961118

2/9/11 (Item 11 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10662852 97011573 PMID: 8858583

The clp (CS31A) operon is negatively controlled by Lrp, ClpB, and L-alanine at the transcriptional level.

Martin C

Laboratoire de Microbiologie, Institut National de la Recherche Agronomique, Saint-Genes-Champanelie, France. cmartin@clermont.inra.fr

Molecular microbiology (ENGLAND) Jul 1996, 21 (2) p281-92, ISSN 0950-382X Journal Code: 8712028

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Biosynthesis of the Escherichia coli CS31A surface antigen was subject to phase-variation control and repressed by L-alanine. Nucleotide sequence analysis of the clp operon, encoding the biosynthesis of CS31A, revealed the presence of a regulatory gene, clpB. The amino acid sequence of the regulatory protein ClpB showed similarity to the primary structure of PapB, FaeB and AfaA, involved in the regulation of expression of Pap, K88, and Afa-3 fimbriae, respectively. The clp regulatory region contained two deoxyadenosine methylase sites (**GATC** -I and **GATC** -II). The leucine-responsive regulatory protein (Lrp) was required for specific methylation **inhibition** of the **GATC** -II site. The activity of the clp promoter was monitored in a clp-lacZYA single-copy fusion. The cloned DNA used in this study did not contain a related papI gene. In these conditions, we showed, as expected, that phase variation did not occur. However, transcription of the clp operon was negatively controlled by ClpB and Lrp, and was maximal in the absence of **Dam** methylase. In the presence of AfaF, a PapI equivalent, the phase-variation control was restored. We concluded that two regulatory mechanisms were superimposed to control the clp expression. Phase variation, mediated by Lrp and a PapI equivalent, controlled the number of cells producing CS31A in a single colony. The second mechanism, described in this report, was mediated by ClpB and Lrp and controls the level of CS31A produced by a single cell. Furthermore, we showed that L-alanine reduced, by about twofold, the clp promoter activity independently of a PapI equivalent, ClpB, Lrp or Dam methylase. In addition, the presence of L-alanine prevented the phase-variation control mediated by AfaF.

Tags: Comparative Study

Descriptors: *Bacterial Proteins--genetics--GE; *Operon; Alanine --pharmacology--PD; Amino Acid Sequence; Base Sequence; Chromosome Mapping; DNA, Bacterial--genetics--GE; DNA-Binding Proteins--genetics--GE; Escherichia coli--genetics--GE; Escherichia coli--immunology--IM; Escherichia coli--metabolism--ME; Gene Expression Regulation, Bacterial --drug effects--DE; Genes, Bacterial; Genes, Regulator; Heat-Shock Proteins

--genetics--GE; Leucine--pharmacology--PD; Molecular Sequence Data; Operon --immunology--IM; Sequence Homology, Amino Acid; Site-Specific DNA-Methyltransferase (Adenine-Specific)--metabolism--ME; Transcription, Genetic--drug effects--DE
Molecular Sequence Databank No.: GENBANK/L48184
CAS Registry No.: 0 (Bacterial Proteins); 0 (DNA, Bacterial); 0 (DNA-Binding Proteins); 0 (Heat-Shock Proteins); 0 (heat-shock protein F84.1); 138791-20-5 (leucine-responsive regulatory protein); 144998-09-4 (clpG protein); 56-41-7 (Alanine); 61-90-5 (Leucine)
Enzyme No.: EC 2.1.1.- (Dam methyltransferase); EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific))
Record Date Created: 19970225
Record Date Completed: 19970225

2/9/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10604562 96422150 PMID: 8824767
Importance of the replication origin sequestration in cell division of Escherichia coli.
Meury J; Bahloul A; Kohiyama M
Biochimie Genetique, Universite Paris, France.
Biochimie (FRANCE) 1995, 77 (11) p875-9, ISSN 0300-9084
Journal Code: 1264604
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
The DNA adenine **methyltransferase** of Escherichia coli methylates adenines at **GATC** sequences. The mutant deficient in this methylase has no apparent deficiency in the cell division process in spite of the absence of both synchrony in initiations of chromosomal DNA replication and sequestration of replication origin (oriC) at hemimethylated state. However, the **dam** mutant cannot resume cell division after hyperosmotic shock differing from the wild-type strain. This **inhibition** is not provoked by induction of the cell division **inhibitor** , SfiA protein. Although the FtsZ protein is present in the **dam** mutant in a reduced amount compared to wild-type, the quantitative difference of this protein is not the main reason of division arrest provoked by hyperosmotic shock. This observation supports the idea of oriC-membrane interaction playing a role both in chromosome partitioning and cell division as predicted by replicon theory.
Tags: Support, Non-U.S. Gov't
Descriptors: *Bacterial Proteins--metabolism--ME; *DNA, Bacterial --genetics--GE; *Escherichia coli--genetics--GE; *Escherichia coli--growth and development--GD; *Replication Origin--physiology--PH; Bacterial Proteins--genetics--GE; Betaine--pharmacology--PD; Cell Division; Mutation
CAS Registry No.: 0 (Bacterial Proteins); 0 (DNA, Bacterial); 0 (FtsZ protein); 0 (sulA protein, E coli); 107-43-7 (Betaine)
Record Date Created: 19961205
Record Date Completed: 19961205

2/9/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10310697 96112794 PMID: 8846772
Differential binding of Lrp to two sets of pap DNA binding sites mediated by Pap I regulates Pap phase variation in Escherichia coli.
Nou X; Braaten B; Kaltenbach L; Low D A
Department of Pathology, University of Utah, Salt Lake City 84132, USA.
EMBO journal (ENGLAND) Dec 1 1995, 14 (23) p5785-97, ISSN 0261-4189
Journal Code: 8208664
Contract/Grant No.: 2R01 AI23348; AI; NIAID
Document type: Journal Article

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Pyelonephritis-associated pili (Pap) expression in Escherichia coli is subject to a phase variation control mechanism that is regulated by the leucine-responsive regulatory protein (Lrp), PapI, and deoxyadenosine methylase (**Dam**). In previous work, we found that the differential **Dam** methylation of two target sites in pap regulatory DNA, **GATC** -I and **GATC** II, is essential for the transition between active and inactive pap transcriptional states. Here, we identify six Lrp binding sites within the pap regulatory DNA, each separated by about three helical turns. Lrp binds with highest affinity to three sites (1, 2 and 3) proximal to the papBAp promoter. A mutational analysis indicates that the binding of Lrp to sites 2 and 3 **inhibits** pap transcription, which is consistent with the fact that Lrp binding site 3 is located between the --35 and --10 RNA polymerase binding region of papBAp. The addition of PapI decreases the affinity of Lrp for sites 1, 2 and 3 and increases its affinity for the distal Lrp binding sites 4 and 5. Mutations within Lrp binding sites 4 and 5 shut off pap transcription, indicating that the binding of Lrp to this pap region activates pap transcription. The pap **GATC** -I and **GATC** -II methylation sites are located within Lrp binding sites 5 and 2, respectively, providing a mechanism by which **Dam** controls Lrp binding and Pap phase variation.

Tags: Support, U.S. Gov't, P.H.S.

Descriptors: *Bacterial Proteins--metabolism--ME; *DNA, Bacterial --metabolism--ME; *DNA-Binding Proteins--metabolism--ME; *Escherichia coli --genetics--GE; *Fimbriae, Bacterial--genetics--GE; *Transcription Factors --metabolism--ME; Bacterial Proteins--genetics--GE; Base Sequence; Binding Sites; DNA Footprinting; DNA, Bacterial--genetics--GE; DNA-Binding Proteins --genetics--GE; Escherichia coli--ultrastructure--UL; Gene Expression Regulation, Bacterial--genetics--GE; Methylation; Models, Genetic; Molecular Sequence Data; Mutagenesis, Site-Directed--genetics--GE; Nucleic Acid Conformation; Phenotype; Site-Specific DNA-Methyltransferase (Adenine-Specific)--metabolism--ME; Transcription Factors--genetics--GE; Transcription, Genetic--genetics--GE

CAS Registry No.: 0 (Bacterial Proteins); 0 (DNA, Bacterial); 0 (DNA-Binding Proteins); 0 (PapI protein); 0 (Transcription Factors); 138791-20-5 (leucine-responsive regulatory protein)

Enzyme No.: EC 2.1.1.- (Dam methyltransferase); EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific))

Record Date Created: 19961021
Record Date Completed: 19961021

2/9/25 (Item 25 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08579533 95267835 PMID: 7748925

On the role of the Escherichia coli integration host factor (IHF) in repression at a distance of the pyrimidine specific promoter P1 of the carAB operon.

Charlier D; Huysveld N; Roovers M; Glansdorff N
Research Institute of the CERIA-COOVI, Brussels, Belgium.

Biochimie (FRANCE) 1994, 76 (10-11) p1041-51, ISSN 0300-9084
Journal Code: 1264604
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Binding of integration host factor to its target site, centered around nucleotide -305 upstream of the transcription startpoint, exerts **antagonistic** effects on the expression of P1, the upstream pyrimidine specific promoter of the E coli and S typhimurium carAB operons. IHF stimulates P1 promoter activity in minimal medium, but also increases the repressibility of this promoter by pyrimidines. We present evidence strongly suggesting that IHF exerts these effects by **modulating** the binding of another pyrimidine specific regulatory molecule, probably the

product of gene carP. The carAB control region contains a **GATC** **Dam** methylation site, 106 bp upstream of the P1 transcription startpoint, which can be protected in vivo against methylation. This protection requires at least the regulatory carP gene product and a high pyrimidine nucleotide pool and, as shown here, the integration host factor. Whether CarP directly binds to this site or exerts its protective effect indirectly is not yet known. In the absence of IHF (himA) or in mutants affected in the IHF target site this protection is strongly impaired, suggesting that IHF positively influences the formation or the stability of the protective protein-DNA complex some 200 bp downstream. Furthermore, we have demonstrated that the distance separating the IHF and **GATC** **Dam** methylase target sites is crucial for the in vivo protection and for pyrimidine mediated regulation of P1 promoter expression. Indeed, shortening this distance by 6 bp, and more surprisingly also by 11 bp, results in a severe reduction of the degree of in vivo protection of the **GATC** site against methylation and concomitantly of the repressibility by pyrimidines of P1 promoter activity. The absence of both these effects in a double, deletion-duplication, mutant resulting in a net increase of the intervening sequence by 1 bp, clearly demonstrates that these effects are not due to the disruption of an important regulatory site, but must be attributed to variations in the distance separating different protein binding sites.

Tags: Support, Non-U.S. Gov't

Descriptors: *Bacterial Proteins--genetics--GE; *DNA-Binding Proteins --genetics--GE; *Escherichia coli--genetics--GE; *Operon; *Promoter Regions (Genetics); *Repressor Proteins--genetics--GE; Base Sequence; Methylation; Methyltransferases--genetics--GE; Molecular Sequence Data; Pyrimidine Nucleotides--genetics--GE

CAS Registry No.: 0 (Bacterial Proteins); 0 (DNA-Binding Proteins); 0 (Pyrimidine Nucleotides); 0 (Repressor Proteins)

Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.- (Dam methyltransferase)

Gene Symbol: carAB

Record Date Created: 19950622

Record Date Completed: 19950622

2/9/27 (Item 27 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

08188797 94254718 PMID: 7910935

Leucine-responsive regulatory protein and deoxyadenosine methylase control the phase variation and expression of the sfa and daa pili operons in Escherichia coli.

van der Woude M W; Low D A

Department of Pathology, University of Utah School of Medicine, Salt Lake City 84132.

Molecular microbiology (ENGLAND) Feb 1994, 11 (4) p605-18, ISSN 0950-382X Journal Code: 8712028

Contract/Grant No.: 2R01 AI23348; AI; NIAID; 5K04 AI881; AI; NIAID

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The Escherichia coli operons daa and sfa encode F1845 and S pili, respectively. In this paper we show that the expression of these operons is under phase variation control at a transcriptional level. The transcription of both operons is dependent on the global regulator leucine-responsive regulatory protein (Lrp) and deoxyadenosine methylase (**Dam**). Lrp is required for methylation protection of two **GATC** sites located within conserved DNA sequences in the regulatory regions of these operons. These **GATC** sites are differentially methylated, establishing a methylation pattern which is characteristic of either the phase ON or phase OFF state. We also show that Lrp binds to the daa and sfa regulatory regions and that this binding is **modulated** by the methylation of the **GATC** sites. These results indicate that the phase variation of the daa and sfa operons is regulated by a mechanism involving differential binding of Lrp owing to

methylation of **GATC** sites in the regulatory region, which is similar to the mechanism that controls phase variation of the pap operon.

Tags: Support, U.S. Gov't, P.H.S.

Descriptors: *Bacterial Proteins--metabolism--ME; *Bacterial Proteins --physiology--PH; *DNA, Bacterial--genetics--GE; *DNA-Binding Proteins --physiology--PH; *Escherichia coli--genetics--GE; *Fimbriae, Bacterial --metabolism--ME; *Gene Expression Regulation, Bacterial; *Methyltransferases--physiology--PH; *Operon; Bacterial Proteins --biosynthesis--BI; Bacterial Proteins--genetics--GE; Base Sequence; DNA, Bacterial--metabolism--ME; Escherichia coli--metabolism--ME; Methylation; Molecular Sequence Data; Recombinant Fusion Proteins--biosynthesis--BI; Regulatory Sequences, Nucleic Acid

CAS Registry No.: 0 (Bacterial Proteins); 0 (DNA, Bacterial); 0 (DNA-Binding Proteins); 0 (DaaA protein); 0 (DaaF protein); 0 (PapI protein); 0 (Recombinant Fusion Proteins); 0 (sfaB protein, E coli); 0 (sfaC protein, E coli); 138791-20-5 (leucine-responsive regulatory protein); 147277-51-8 (sfaA protein, E coli)

Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.- (Dam methyltransferase)

Record Date Created: 19940630

Record Date Completed: 19940630

2/9/33 (Item 33 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

07427672 92291095 PMID: 1601880

Initiation of methyl-directed mismatch repair.

Au K G; Welsh K; Modrich P

Department of Biochemistry, Duke University Medical Center, Durham, North Carolina 27710.

Journal of biological chemistry (UNITED STATES) Jun 15 1992, 267 (17) p12142-8, ISSN 0021-9258 Journal Code: 2985121R

Contract/Grant No.: GM23719; GM; NIGMS

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Escherichia coli MutH possesses an extremely weak d(GATC) endonuclease that responds to the state of methylation of the sequence (Welsh, K. M., Lu, A.-L., Clark, S., and Modrich, P. (1987) J. Biol. Chem. 262, 15624-15629). MutH endonuclease is activated in a reaction that requires MutS, MutL, ATP, and Mg2+ and depends upon the presence of a mismatch within the DNA. The degree of activation correlates with the efficiency with which a particular mismatch is subject to methyl-directed repair (G-T greater than G-G greater than A-C greater than C-C), and activated MutH responds to the state of DNA adenine methylation. Incision of an unmethylated strand occurs immediately 5' to a d(**GATC**) sequence, leaving 5' phosphate and 3' hydroxy termini (pN decreases pGpAp-TpC). Unmethylated d(**GATC**) sites are subject to double strand cleavage by activated MutH, an effect that may account for the killing of **dam** - mutants by 2-aminopurine. The mechanism of activation apparently requires ATP hydrolysis since adenosine-5'-O-(3-thiotriphosphate) not only fails to support the reaction but also **inhibits** activation promoted by ATP. The process has no obligate polarity as d(**GATC**) site incision by the activated nuclease can occur either 3' or 5' to the mismatch on an unmethylated strand. However, activation is sensitive to DNA topology. Circular heteroduplexes are better substrates than linear molecules, and activity of DNAs of the latter class depends on placement of the mismatch and d(**GATC**) site within the molecule. MutH activation is supported by a 6-kilobase linear heteroduplex in which the mismatch and d(GATC) site are centrally located and separated by 1 kilobase, but a related molecule, in which the two sites are located near opposite ends of the DNA, is essentially inactive as substrate. We conclude that MutH activation represents the initiation stage of methyl-directed repair and suggest that interaction of a mismatch and a d(GATC) site is provoked by MutS binding to a mispair, with subsequent ATP-dependent translocation of one or more Mut proteins along the helix

leading to cleavage at a d(GATC) sequence on either side of the mismatch.
Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Descriptors: *DNA Repair; *Escherichia coli--genetics--GE; *Nucleic Acid Heteroduplexes; Adenosine Triphosphate--analogs and derivatives--AA; Adenosine Triphosphate--metabolism--ME; Bacterial Proteins--metabolism--ME; Base Sequence; Cations, Divalent; DNA, Bacterial--genetics--GE; DNA, Bacterial--metabolism--ME; DNA-Binding Proteins--metabolism--ME; Electrophoresis, Polyacrylamide Gel; Endodeoxyribonucleases--metabolism--ME; Genes, Bacterial; Hydrolysis; Magnesium--metabolism--ME; Methylation; Molecular Sequence Data; Nucleic Acid Conformation; Substrate Specificity
CAS Registry No.: 0 (Bacterial Proteins); 0 (Cations, Divalent); 0 (DNA, Bacterial); 0 (DNA-Binding Proteins); 0 (MutS protein); 0 (Nucleic Acid Heteroduplexes); 35094-46-3 (adenosine 5'-O-(3-thiotriphosphate)); 56-65-5 (Adenosine Triphosphate); 7439-95-4 (Magnesium)
Enzyme No.: EC 3.1.- (Endodeoxyribonucleases); EC 3.1.21.- (MutH gene product)
Record Date Created: 19920716
Record Date Completed: 19920716

2/9/35 (Item 35 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07371801 92234969 PMID: 1569034
Escherichia coli cells lacking methylation- blocking **factor (leucine-responsive regulatory protein) have precise timing of initiation of DNA replication in the cell cycle.**
Smith D W; Stine W B; Svitil A L; Bakker A; Zyskind J W
Department of Biology, University of California, San Diego, La Jolla 92093.
Journal of bacteriology (UNITED STATES) May 1992, 174 (9) p3078-82, ISSN 0021-9193 Journal Code: 2985120R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
A protein that is required for specific methylation **inhibition** of two **GATC** sites in the papBA pilin promoter region, known as methylation-**blocking** factor (Mbf) and recently shown to be identical to the leucine-responsive regulatory protein (Lrp), is not responsible for the delayed methylation at oriC implicated in an eclipse period following initiation of DNA replication. Cells containing a transposon mutation within the mbf (lrp) gene initiate DNA replication at the correct time during the cell cycle, whereas cells with increased amounts of the **Dam methyltransferase** initiate DNA replication randomly throughout the cell cycle.
Tags: Support, U.S. Gov't, Non-P.H.S.
Descriptors: *Bacterial Proteins--genetics--GE; *Cell Cycle--genetics--GE; *DNA Replication--genetics--GE; *DNA-Binding Proteins--genetics--GE; *Escherichia coli--genetics--GE; Gene Expression Regulation, Bacterial; Methyltransferases--biosynthesis--BI; Mutation; Time Factors
CAS Registry No.: 0 (Bacterial Proteins); 0 (DNA-Binding Proteins); 138791-20-5 (leucine-responsive regulatory protein)
Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.- (Dam methyltransferase)
Record Date Created: 19920522
Record Date Completed: 19920522

00509816 (USE 9 FOR FULLTEXT)
An Essential Role for DNA Adenine Methylation in Bacterial Virulence
Heithoff, Douglas M.; Sinsheimer, Robert L.; Low, David A.; Mahan, Michael J.<CRF RID="C1">
Department of Molecular, Cellular, and Developmental Biology, University of California, Santa Barbara, CA 93106, USA.
Science Vol. 284 5416 pp. 967
Publication Date: 5-07-1999 (990507) Publication Year: 1999
Document Type: Journal ISSN: 0036-8075
Language: English
Section Heading: REPORTS
Word Count: 2380

(THIS IS THE FULLTEXT)

...Abstract: Dam methylation at specific genomic sites, as evidenced by alterations in DNA methylation patterns. Dam **inhibitors** are likely to have broad **antimicrobial** action, and Dam.sup(-) derivatives of these pathogens may serve as live attenuated vaccines

...Text: latter regulatory mechanism involves formation of heritable DNA methylation patterns, which control gene expression by **modulating** the binding of regulatory proteins. Although Dam regulates pili gene expression, its role in microbial...

...Dam controls the expression of Pap pili by **modulating** the binding of leucine-responsive regulatory protein (Lrp) to pap regulatory DNA sequences (B3) . Lrp...

...to facilitate growth at systemic sites of infection (B12) ; pmrB is involved in resistance to **antibacterial** peptides termed ...2 to 19 (Fig. 2), and this repression was not dependent on the PhoP protein. **Dam** did not significantly affect the expression of the remaining four PhoP-activated genes (B17) . These...

...regulatory proteins to DNA can form DNA methylation patterns by blocking the methylation of specific **Dam** target sites (**GATC** sequences) (B18) . Therefore, we further investigated the interactions between **Dam** and PhoP by determining whether the binding of PhoP (or a PhoP-regulated protein) to specific DNA sites blocks methylation of these sites by **Dam** , resulting in an alteration in the DNA methylation pattern. Analysis of PhoP.sup(+) and PhoP...
...of genomic DNA from PhoP.sup(-) bacteria with Mbo I (which cleaves only at nonmethylated **GATC** sites) resulted in the appearance of DNA fragments that were not present in DNA from PhoP.sup(+) bacteria, indicating that the PhoP protein (or a PhoP-regulated gene product) blocks **Dam** methylation at specific **GATC** -containing sites in the Salmonella genome (Fig. 3, arrows). Recent data have shown that although catabolite gene activator protein binds to a DNA sequence containing **GATC** , it does not protect this site from methylation (B18) . Thus, not every protein that binds to a **Dam** target site protects the **GATC** sequence from methylation. It is also possible that PhoP.sup(+) and PhoP.sup(-) strains have different amounts of **Dam** activity, which in turn could affect DNA methylation patterns. However, this regulation does not occur at the transcriptional level because **Dam** does not alter PhoP expression, nor does PhoP alter **Dam** expression (B17) . Further analysis will determine whether these PhoP-protected sites are within regulatory regions...

...In E. coli, almost all **GATC** sites protected from methylation are in 5 (prime) noncoding DNA regions presumably involved in the...

...patterns identified in Salmonella (Fig. 3) are also within gene regulatory regions. Methylation of specific **GATC** sites in the regulatory regions of virulence genes could affect the binding of regulatory proteins ...

...as has been shown for the pap virulence operon in E. coli (B7) (B18) . Similarly, **Dam** methylation could directly or indirectly affect the expression of PhoPQ-regulated genes in S. typhimurium...DNA adenine

methylases are potentially excellent targets for both vaccines and **antimicrobials** . They are highly conserved in many pathogenic bacteria that cause significant morbidity and mortality, such...

...that share common epitopes. Finally, because the Dam methylase is essential for bacterial virulence, Dam **inhibitors** are likely to have broad **antimicrobial** action, hence Dam is a promising target for **antimicrobial** drug development...

11784901 99223486 PMID: 10206981

The glucocorticoid response element II is functionally homologous in rat and human insulin-like growth factor-binding protein-1 promoters.

Schweizer-Groyer G; Jibard N; Neau E; Fortin D; Cadepond F; Baulieu E E; Groyer A

INSERM U.488, Lab hormones, 94276, Le Kremlin-Bicetre Cedex, France. groyer@kb.inserm.fr

Journal of biological chemistry (UNITED STATES) Apr 23 1999, 274 (17) p11679-86, ISSN 0021-9258 Journal Code: 2985121R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

In vivo, insulin-like growth factor-binding protein-1 (IGFBP-1) **modulates** the IGFs' bioavailability and may contribute to their delivery to peripheral tissues. In rat and human hepatocytes, glucocorticoids stimulate IGFBP-1 gene transcription through homologous glucocorticoid response units (GRU). Transfection experiments have shown that one of these, GRU2 (nucleotide (nt) -121 to -85 and nt -111 to -74 in human and rat promoters, respectively), was on its own able to mediate the glucocorticoid response in rat but not in human species (Suwanichkul, A., Allander, S., Morris, S. L. & Powell, D. R. (1994) J. Biol. Chem. 269, 30835-30841, Goswami, R., Lacson, R., Yang, E., Sam, R. & Unterman, T. (1994) Endocrinology 134, 736-743, and Suh, D. S., Ooi, G. T. & Rechler, M. M. (1994) Mol. Endocrinol. 8, 794-805). A close comparison of GRU2 sequences has pointed out a C to A transition in the underlying GREII, which creates a **GATC** tetranucleotide in rat species. This tetranucleotide is submitted to adenosyl methylation (**dam** methylation) in most Escherichia coli bacterial strains, but not in eucaryotic cells. We showed (i) that on its own, the unmethylated rat GRU2 (propagated in **dam** E. coli strains) was inactive, as is the case for its human counterpart (nonsignificant glucocorticoid inductions, 1.48 +/- 0.23 and 1.7 +/- 0.35-fold in Chinese hamster ovary cells, respectively) and (ii) that its adenosyl methylation in standard **dam** + bacterial strains yielded a functional GRU (6.5 +/- 1. 1 and 13.1 +/- 3.9-fold glucocorticoid inductions in Chinese hamster ovary and HepG2 cells, respectively). Transient transfection in HepG2 hepatoma cells clearly showed that the interaction of liver-enriched trans-acting factor(s) with the 5'-overlapping insulin response element does not enable the unmethylated rat GRU2 or the human GRU2 to become responsive to glucocorticoids (nonsignificant 2.21 +/- 0.48 and 1.20 +/- 0.06-fold induction, respectively). Furthermore, we have correlated these functional data with in vitro DNA-protein interaction studies: the dam methylated rat GREII displayed a 2.8-fold higher affinity for the glucocorticoid receptor than its unmethylated counterpart.

Tags: Animal; Human; Support, Non-U.S. Gov't

Descriptors: *Glucocorticoids--pharmacology--PD; *Insulin-Like Growth-Factor Binding Protein 1--genetics--GE; Base Sequence; CHO Cells; DNA Methylation; DNA Primers; Hamsters; Rats; Sequence Homology, Nucleic Acid; Tumor Cells, Cultured

CAS Registry No.: 0 (DNA Primers); 0 (Glucocorticoids); 0 (Insulin-Like Growth-Factor Binding Protein 1)

Record Date Created: 19990520

Record Date Completed: 19990520

2/9/6 (Item 6 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

11635889 99069662 PMID: 9851883

Regulation of uropathogenic Escherichia coli adhesin expression by DNA methylation.

Hale W B; van der Woude M W; Braaten B A; Low D A

Department of Pathology, University of Utah Health Sciences Center, Salt Lake City, Utah, 84132, USA.

Molecular genetics and metabolism (UNITED STATES) Nov 1998, 65 (3)

p191-6, ISSN 1096-7192 Journal Code: 9805456
Contract/Grant No.: 2RO1 AI23348; AI; NIAID; 5P30-CA42014-07; CA; NCI; 5T35HLO7744; HL; NHLBI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Pap pili play an important role in the pathogenesis of upper urinary tract infections by enabling uropathogenic Escherichia coli to adhere to host epithelial cells. Pap pili are coded for by the pyelonephritis-associated pili (pap) operon, which consists of 11 genes required for the expression and assembly of Pap pili. Expression of Pap pili is regulated by a phase variation mechanism in which the pili expression state of the bacterial population is skewed between phase-on (expression positive) and phase-off (expression negative) states. Pap phase variation is controlled by the cooperative binding of leucine-responsive regulatory protein (Lrp) to two sets of Lrp binding sites in the upstream regulatory region of the pap operon. A single **GATC** sequence, which is the target site for deoxyadenosine methylase (**Dam**), is centrally located within each Lrp binding region. **Dam** plays a critical role in the expression of Pap pili via the formation of DNA methylation patterns. Methylation of **GATC** -I reduced the affinity of Lrp for pap DNA by about twofold. Conversely, Lrp specifically **blocked** methylation of pap **GATC** -I in vitro. These data support the hypothesis that Lrp and **Dam** compete for binding to **GATC** -I, and are consistent with previous results indicating that methylation of **GATC** -I is important for stability of the phase-off state. Copyright 1998 Academic Press.

Tags: Support, U.S. Gov't, P.H.S.
Descriptors: *Adhesins, Escherichia coli--genetics--GE; *DNA Methylation; *DNA-Binding Proteins--metabolism--ME; *Escherichia coli--genetics--GE; *Escherichia coli--pathogenicity--PY; Adhesins, Escherichia coli --metabolism--ME; Binding Sites; DNA-Binding Proteins--genetics--GE; Gene Expression Regulation, Bacterial; Operon; Regulatory Sequences, Nucleic Acid; Site-Specific DNA-Methyltransferase (Adenine-Specific)--genetics--GE; Site-Specific DNA-Methyltransferase (Adenine-Specific)--metabolism--ME
CAS Registry No.: 0 (Adhesins, Escherichia coli); 0 (DNA-Binding Proteins); 138791-20-5 (leucine-responsive regulatory protein)
Enzyme No.: EC 2.1.1.- (Dam methyltransferase); EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific))
Record Date Created: 19990204
Record Date Completed: 19990204

2/9/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10671942 97021025 PMID: 8867385

Analysis of nucleotide methylation in DNA from Corynebacterium glutamicum and related species.

Jang K H; Chambers P J; Britz M L
Centre for Bioprocessing and Food Technology, Victoria University of Technology, Melbourne, Australia.

FEMS microbiology letters (NETHERLANDS) Mar 1 1996, 136 (3) p309-15, ISSN 0378-1097 Journal Code: 7705721
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Plasmid DNA (pCSL17) isolated from Corynebacterium glutamicum transformed recipient McrBC+ strains of Escherichia coli with lower efficiency than McrBC- strains, confirming a previous report by Tauch et al. (FEMS Microbiol. Lett. 123 (1994) 343-348) which inferred that C. glutamicum DNA contains methylcytidine. Analysis of nucleotides in C. glutamicum-derived chromosomal and plasmid DNA failed to detect significant levels of methylated adenosine, but methylated cytidine was readily detected. Restriction enzymes which are **inhibited** by the presence of methylcytidine

Nucleic acids research (ENGLAND) Aug 11 1990, 18 (15) p4369-75, ISSN 0305-1048 Journal Code: 0411011
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

The turnover of DNA-adenine-methylase of E. coli strongly decreases when the temperature is lowered. This has allowed us to study the binding of Dam methylase on 14 bp DNA fragments at 0 degrees C by gel retardation in the presence of Ado-Met, but without methylation taking place. The enzyme can bind non-specific DNA with low affinity. Binding to the specific sequence occurs in the absence of S-adenosyl-methionine (Ado-Met), but is activated by the presence of the methyl donor. The two competitive **inhibitors** of Ado-Met, sinefungin and S-adenosyl-homocysteine, can neither activate this binding to DNA by themselves, nor **inhibit** this activation by Ado-Met. This suggests that Ado-Met could bind to **Dam** methylase in two different environments. In one of them, it could play the role of an allosteric effector which would reinforce the affinity of the enzyme for the **GATC** site. The analogues can not compete for such binding. In the other environment Ado-Met would be in the catalytic site and could be exchanged by its analogues. We have also visualized conformational changes in **Dam** methylase induced by the simultaneous binding of Ado-Met and the specific target sequence of the enzyme, by an anomaly of migration and partial resistance to proteolytic treatment of the ternary complex Ado-Met/ **Dam** methylase/ **GATC** .

Tags: Support, Non-U.S. Gov't
Descriptors: *Escherichia coli--enzymology--EN; *Methyltransferases --metabolism--ME; *S-Adenosylmethionine--metabolism--ME; Adenosine--analogs and derivatives--AA; Adenosine--pharmacology--PD; Allosteric Regulation; Base Sequence; Binding Sites; Binding, Competitive; DNA, Bacterial --metabolism--ME; Kinetics; Methylation; Models, Molecular; Molecular Sequence Data; Protein Conformation; S-Adenosylhomocysteine--pharmacology --PD; S-Adenosylmethionine--pharmacology--PD; Sodium Chloride--pharmacology --PD; Temperature; Thermodynamics
CAS Registry No.: 0 (DNA, Bacterial); 29908-03-0 (S-Adenosylmethionine); 58-61-7 (Adenosine); 58944-73-3 (sinefungin); 7647-14-5 (Sodium Chloride); 979-92-0 (S-Adenosylhomocysteine)
Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.- (Dam methyltransferase)
Record Date Created: 19900924
Record Date Completed: 19900924

2/9/41 (Item 41 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05597977 87277349 PMID: 3301526
Spontaneous mutations occur near dam recognition sites in a dam- Escherichia coli host.
Carraway M; Youderian P; Marinus M G
Genetics (UNITED STATES) Jul 1987, 116 (3) p343-7, ISSN 0016-6731 Journal Code: 0374636
Contract/Grant No.: GM33233; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

The mismatch repair system of Escherichia coli K12 removes mispaired bases from DNA. Mismatch repair can occur on either strand of DNA if it lacks N6-methyladenines within 5'- **GATC** -3' sequences. In hemimethylated heteroduplexes, repair occurs preferentially on the unmethylated strand. If both strands are fully methylated, repair is **inhibited** . Mutant (**dam** -) strains of E. coli defective in the adenine methylase that recognizes 5'- **GATC** -3' sequences (**Dam**), and therefore defective in mismatch repair, show increased spontaneous mutation rates compared to otherwise isogenic **dam** + hosts. We have isolated and characterized 91 independent mutations

2/9/37 (Item 37 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06913825 91154136 PMID: 1671857

Evidence for a methylation- blocking factor (mbf) locus involved in pap pilus expression and phase variation in Escherichia coli.

Braaten B A; Blyn L B; Skinner B S; Low D A
Department of Pathology, University of Utah Medical Center, Salt Lake City 84132.

Journal of bacteriology (UNITED STATES) Mar 1991, 173 (5) p1789-800, ISSN 0021-9193 Journal Code: 2985120R
Contract/Grant No.: 5T32-GM07464; GM; NIGMS; AI00881; AI; NIAID; AI23348; AI; NIAID
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Transcription of the pyelonephritis-associated pilus (pap) operon of Escherichia coli is subject to regulation by a phase variation control mechanism in which the pap pilin gene alternates between transcriptionally active (phase-on) and inactive (phase-off) states. Pap phase variation appears to involve differential **inhibition** of deoxyadenosine methylase (**Dam**) methylation of two pap **GATC** sites, GATC1028 and GATC1130, located in the regulatory region upstream of the papBA promoter. DNA from phase-on cells contains an unmethylated adenosine in the GATC1028 site, whereas DNA from phase-off cells contains an unmethylated adenosine in the GATC1130 site. papI and papB are two regulatory genes in the pap operon. Analysis of pap deletion mutants suggests that papI is required for methylation **inhibition** at the GATC1028 site; however, neither papI nor papB is required for **inhibition** of methylation at the GATC1130 site. We have identified a chromosomal locus, mbf (methylation- **blocking** factor), that is required for methylation protection of both the pap GATC1028 and GATC1130 sites. The mbf locus was identified after transposon mTn10 mutagenesis and mapped to 19.6 min on the E. coli chromosome. The effect of transposon mutations within mbf on pap pilin transcription was determined by using a papBAp-lac operon fusion which places lacZ under control of the papBA promoter. E. coli containing mbf::mTn10 and phase-off mbf+ E. coli cells both expressed beta-galactosidase levels about 30-fold lower than the beta-galactosidase level measured for phase-on mbf+ E. coli cells. These results indicated that mbf was necessary for pap pilin transcription and were supported by Northern (RNA) blotting and primer extension analyses.(ABSTRACT TRUNCATED AT 250 WORDS)

Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Descriptors: *Bacterial Outer Membrane Proteins--genetics--GE; *Biological Factors--genetics--GE; *Escherichia coli--genetics--GE; *Fimbriae, Bacterial--physiology--PH; *Operon; Amino Acid Sequence; Bacteriophage lambda--genetics--GE; Base Sequence; DNA, Bacterial--genetics --GE; Escherichia coli--physiology--PH; Fimbriae Proteins; Methylation; Molecular Sequence Data; Mutagenesis, Insertional; Plasmids; Promoter Regions (Genetics); Restriction Mapping
CAS Registry No.: 0 (Bacterial Outer Membrane Proteins); 0 (Biological Factors); 0 (DNA, Bacterial); 0 (Plasmids); 147680-16-8 (Fimbriae Proteins)
Record Date Created: 19910408
Record Date Completed: 19910408

2/9/39 (Item 39 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06730331 90356368 PMID: 2201947

The double role of methyl donor and allosteric effector of S-adenosyl-methionine for Dam methylase of E. coli.

Bergerat A; Guschlbauer W
Departement de Biologie, Centre d'Etudes Nucleaires de Saclay, Gif-sur-Yvette, France.

STIC-ILL

From: Portner, Ginny
Sent: Wednesday, August 13, 2003 9:57 AM
To: STIC-ILL
Subject: methyltransferase

1645

EQUENCE FROM NUCLEIC ACID.
MEDLINE=83168905; PubMed=6300769; [NCBI, ExPASy, EBI, Israel, Japan]
Brooks J.E., Blumenthal R.M., Gingeras T.R.;
"The isolation and characterization of the Escherichia coli DNA adenine methylase (dam) gene.";
Nucleic Acids Res. 11:837-851(1983).
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SEQUENCE FROM NUCLEIC ACID.
MEDLINE=95327050; PubMed=7603433; [NCBI, ExPASy, EBI, Israel, Japan]
Lyngstadaas A., Lobner-Olesen A., Boye E.;
"Characterization of three genes in the dam-containing operon of Escherichia coli.";
Mol. Gen. Genet. 247:546-554(1995).

SEQUENCE OF 1-18 FROM NUCLEIC ACID.
STRAIN=K12;
MEDLINE=89364696; PubMed=2549371; [NCBI, ExPASy, EBI, Israel, Japan]
Jonczyk P., Hines R., Smith D.W.;
"The Escherichia coli dam gene is expressed as a distal gene of a new operon.";
Mol. Gen. Genet. 217:85-96(1989).
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MUTAGENESIS.
MEDLINE=93341922; PubMed=8341592; [NCBI, ExPASy, EBI, Israel, Japan]
Guyot J.-B., Grassi J., Hahn U., Guschlbauer W.;
"The role of the preserved sequences of Dam methylase.";
Nucleic Acids Res. 21:3183-3190(1993).

SEQUENCE FROM NUCLEIC ACID.
SPECIES=S.typhimurium;
MEDLINE=98241341; PubMed=9575240; [NCBI, ExPASy, EBI, Israel, Japan]
Brawer R., Batista F.D., Burrone O.R., Sordelli D.O., Cerquetti M.C.;
"A temperature-sensitive DNA adenine methyltransferase mutant of Salmonella typhimurium.";
Arch. Microbiol. 169:530-533(1998).
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SEQUENCE FROM NUCLEIC ACID.
SPECIES=S.typhimurium;
STRAIN=LT2 / SGSC1412 / ATCC 700720;
MEDLINE=21534948; PubMed=11677609; [NCBI, ExPASy, EBI, Israel, Japan]
McClelland M., Sanderson K.E., Spieth J., Clifton S.W., Latreille P., Courtney L., Porwollik S., Ali J., Dante M., Du F., Hou S., Layman D., Leonard S., Nguyen C., Scott K., Holmes A., Grewal
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"Complete genome sequence of Salmonella enterica serovar Typhimurium LT2.";
Nature 413:852-856(2001).
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SPECIES=S.typhi;
STRAIN=CT18;
MEDLINE=21534947; PubMed=11677608; [NCBI, ExPASy, EBI, Israel, Japan]
Parkhill J., Dougan G., James K.D., Thomson N.R., Pickard D., Wain J., Churcher C., Mungall K.L., Bentley S.D., Holden M.T.G., Sebaihia M., Baker S., Basham D., Brooks K., Chillingworth T.,
Connerton P., Cronin A., Davis P., Davies R.M., Dowd L., White N., Farrar J., Feltwell T., Hamlin N., Haque A., Hien T.T., Holroyd S., Jagels K., Krogh A., Larsen T.S., Leather S., Moule S.,
O'Gaora P., Parry C., Quail M., Rutherford K., Simmonds M., Skelton J., Stevens K., Whitehead S., Barrell B.G.;
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Nature 413:848-852(2001).

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MEDLINE=94171081; PubMed=8125341; [NCBI, ExPASy, EBI, Israel, Japan]
Bandyopadhyay R., Das J.;
"The DNA adenine methyltransferase-encoding gene (dam) of Vibrio cholerae.";
Gene 140:67-71(1994).
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SEQUENCE FROM NUCLEIC ACID.

STRAIN=Classical Ogawa 395 / ATCC 39541 / Serotype O1;
MEDLINE=21562622; PubMed=11705940; [NCBI, ExPASy, EBI, Israel, Japan]
Julio S.M., Heithoff D.M., Provenzano D., Klose K.E., Sinsheimer R.L., Low D.A., Mahan M.J.;
"DNA adenine methylase is essential for viability and plays a role in the pathogenesis of Yersinia pseudotuberculosis and Vibrio cholerae.";
Infect. Immun. 69:7610-7615(200

STRAIN=Nichols;
MEDLINE=98005685; PubMed=9345771; [NCBI, ExPASy, EBI, Israel, Japan]
Stamm L.V., Greene S.R., Barnes N.Y., Bergen H.L., Hardham J.M.;
"Identification and characterization of a Treponema pallidum subsp. pallidum gene encoding a DNA adenine methyltransferase.";
FEMS Microbiol. Lett. 155:115-119(1997).

[2]
SEQUENCE FROM NUCLEIC ACID.
STRAIN=Nichols;
MEDLINE=98332770; PubMed=9665876; [NCBI, ExPASy, EBI, Israel, Japan]
Fraser C.M., Norris S.J., Weinstock G.M., White O., Sutton G.G., Dodson R., Gwinn M., Hickey E.K., Clayton R., Ketchum K.A., Sodergren E., Hardham J.M., McLeod M.P., Salzberg S.,
Peterson J., Khalak H., Richardson D., Howell J.K., Chidambaram M., Utterback T., McDonald L., Artiach P., Bowman C., Cotton M.D., Fujii C., Garland S., Hatch B., Horst K., Roberts K.,
Sandusky M., Weidman J., Smith H.O., Venter J.C.;
"Complete genome sequence of Treponema pallidum, the syphilis spirochete.";
Science 281:375-388(1998).

SEQUENCE FROM NUCLEIC ACID.
STRAIN=Sr41;
MEDLINE=99315777; PubMed=10383952; [NCBI, ExPASy, EBI, Israel, Japan]
Ostendorf T., Cherepanov P., de Vries J., Wackernagel W.;
"Characterization of a dam mutant of Serratia marcescens and nucleotide sequence of the dam region.";
J. Bacteriol. 181:3880-3885(1999).

STRAIN=WR302;
MEDLINE=97465963; PubMed=9321671; [NCBI, ExPASy, EBI, Israel, Japan]
Gunn J.S., Stein D.C.;
"The Neisseria gonorrhoeae S.NgoVIII restriction/modification system: a type IIs system homologous to the Haemophilus parahaemolyticus HphI restriction/modification system.";
Nucleic Acids Res. 25:4147-4152(1997).

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STRAIN=Classical Ogawa 395 / ATCC 39541 / Serotype O1;
MEDLINE=21562622; PubMed=11705940; [NCBI, ExPASy, EBI, Israel, Japan]
Julio S.M., Heithoff D.M., Provenzano D., Klose K.E., Sinsheimer R.L., Low D.A., Mahan M.J.;
"DNA adenine methylase is essential for viability and plays a role in the pathogenesis of Yersinia pseudotuberculosis and Vibrio cholerae.";
Infect. Immun. 69:7610-7615(200

STRAIN=Nichols;
MEDLINE=98005685; PubMed=9345771; [NCBI, ExPASy, EBI, Israel, Japan]
Stamm L.V., Greene S.R., Barnes N.Y., Bergen H.L., Hardham J.M.;
"Identification and characterization of a Treponema pallidum subsp. pallidum gene encoding a DNA adenine methyltransferase.";
FEMS Microbiol. Lett. 155:115-119(1997).
[2]
SEQUENCE FROM NUCLEIC ACID.
STRAIN=Nichols;
MEDLINE=98332770; PubMed=9665876; [NCBI, ExPASy, EBI, Israel, Japan]
Fraser C.M., Norris S.J., Weinstock G.M., White O., Sutton G.G., Dodson R., Gwinn M., Hickey E.K., Clayton R., Ketchum K.A., Sodergren E., Hardham J.M., McLeod M.P., Salzberg S.,
Peterson J., Khalak H., Richardson D., Howell J.K., Chidambaram M., Utterback T., McDonald L., Artiach P., Bowman C., Cotton M.D., Fujii C., Garland S., Hatch B., Horst K., Roberts K.,
Sandusky M., Weidman J., Smith H.O., Venter J.C.;
"Complete genome sequence of Treponema pallidum, the syphilis spirochete.";
Science 281:375-388(1998).

SEQUENCE FROM NUCLEIC ACID.
STRAIN=Sr41;
MEDLINE=99315777; PubMed=10383952; [NCBI, ExPASy, EBI, Israel, Japan]
Ostendorf T., Cherepanov P., de Vries J., Wackernagel W.;
"Characterization of a dam mutant of Serratia marcescens and nucleotide sequence of the dam region.";
J. Bacteriol. 181:3880-3885(1999).

STRAIN=WR302;
MEDLINE=97465963; PubMed=9321671; [NCBI, ExPASy, EBI, Israel, Japan]
Gunn J.S., Stein D.C.;
"The Neisseria gonorrhoeae S.NgoVIII restriction/modification system: a type IIs system homologous to the Haemophilus parahaemolyticus HphI restriction/modification system.";
Nucleic Acids Res. 25:4147-4152(1997).

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08672457 95361056 PMID: 7634390

Mutations in the Ada O6-alkylguanine-DNA alkyltransferase conferring sensitivity to inactivation by O6-benzylguanine and 2,4-diamino-6-benzyloxy-5-nitrosopyrimidine.

Crone T M; Kanugula S; Pegg A E

Department of Cellular and Molecular Physiology, Milton S. Hershey Medical Center, Pennsylvania State University College of Medicine, Hershey 17033, USA.

Carcinogenesis (ENGLAND) Aug 1995, 16 (8) p1687-92, ISSN 0143-3334 Journal Code: 8008055

Contract/Grant No.: CA-18137; CA; NCI; CA-57725; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Although the human O6-alkylguanine-DNA alkyltransferase (AGT) is very sensitive to inactivation by O6-benzylguanine (BG) or 2,4-diamino-6-benzyloxy-5-nitrosopyrimidine (5-nitroso-BP), the equivalent protein formed by the carboxyl terminal domain of the product of the Escherichia **coli** ada gene (Ada-C) is unaffected by these **inhibitors** . This difference is remarkable in view of the substantial similarity between these proteins (33% of the residues in the common sequence are identical) and is potentially very important since these **inhibitors** are under development as drugs to enhance the anti-tumor activity of alkylating agents. In order to understand the reason for the resistance of the Ada-C protein, we have made chimeras between Ada-C and AGT sequences and mutations in the Ada-C protein, expressed the altered proteins in an E. **coli** strain lacking endogenous alkyltransferase activity and tested the **inactivation** of the resulting proteins by BG or 5-nitroso-BP. Chimeric alkyltransferase proteins were made in which the residues on the amino side of the cysteine acceptor site came from Ada-C and the residues on the carboxyl side came from AGT and vice versa but these did not show sensitivity to BG suggesting that resistance is produced by residues in both segments of the protein. Analysis of the Ada-C mutant proteins revealed two sites for mutations that confer sensitivity to these **inhibitors** . One of these was tryptophan-336 and the other was residues lysine-314 and alanine-316. Thus, when the combined mutations of A316P/W336A were made in the Ada-C sequence, the protein was sensitive to **inactivation** by BG. This A316P/W336A mutant protein was even more sensitive to 5-nitroso-BP and the mutant proteins W336A, K314P/A316P and A316P could also be **inhibited** by this drug (in decreasing order of sensitivity) although the control Ada-C and a mutant R335S were not **inhibited** . These results provide strong support for the hypothesis that the resistance of the Ada-C alkyl-transferase is due to a steric effect limiting access to the active site. Insertion of proline residues at positions 314 and 316 and removal of the bulky tryptophan residue at position 336 increases the space available at the active site and permits these **inhibitors** to be effective.

Tags: Support, U.S. Gov't, P.H.S.

Descriptors: *Guanine--analogs and derivatives--AA; *Methyltransferases --antagonists and inhibitors--AI; Amino Acid Sequence; Bacterial Proteins --antagonists and inhibitors--AI; Base Sequence; Binding Sites; Guanine --pharmacology--PD; Molecular Sequence Data; Mutation; O(6)-Methylguanine-DNA Methyltransferase; Structure-Activity Relationship

CAS Registry No.: 0 (Ada regulatory protein, E coli); 0 (Bacterial Proteins); 19916-73-5 (O(6)-benzylguanine); 73-40-5 (Guanine)

Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.63 (O(6)-Methylguanine-DNA Methyltransferase)

Record Date Created: 19950914

Record Date Completed: 19950914

7/9/21
DIALOG(R)File 155:MEDLINE(R)

05411627 87090122 PMID: 3099190

Induction of SOS and adaptive responses by alkylating agents in Escherichia coli mutants deficient in 3-methyladenine-DNA glycosylase activities.

Costa de Oliveira R; Laval J; Boiteux S

Mutation research (NETHERLANDS) Jan 1987, 183 (1) p11-20, ISSN 0027-5107 Journal Code: 0400763
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

The induction of SOS and adaptive responses by alkylating agents was studied in Escherichia **coli** mutants tagA and alkA deficient in 3-methyladenine-DNA glycosylase activities. The SOS response was measured using an sfiA::lacZ operon fusion. The sfiA operon, in the double mutant tagA alkA, is induced at 5-50-fold lower concentrations of all tested methylating and ethylating compounds, as compared to the wild-type strain. In all cases, the tagA mutation, which **inactivates** the constitutive and specific 3-alkyladenine-DNA glycosylase I (TagI), sensitizes the strain to the SOS response. The sensitization effect of alkA mutation, which **inactivates** the inducible 3-alkyladenine-DNA glycosylase II (TagII), is observed under conditions which allow the induction of the adaptive response. We conclude that the persistence of 3-methyladenine and 3-ethyladenine residues in DNA most likely leads to the induction of the SOS functions. In contrast, the adaptive response, evaluated by O6-methylguanine-DNA methyltransferase activity in cell extracts, was not affected by either tagA or alkA mutations. The results suggest that the SOS and adaptive responses use different alkylation products as an inducing "signal". However, adaptation protein TagII **inhibits** the induction of the SOS response to some extent, due to its action at the level of signal production. Finally, we provide conditions to improve short-term **bacterial** tests for the detection of genotoxic alkylating agents.

Tags: Support, Non-U.S. Gov't
Descriptors: Adaptation, Biological--drug effects--DE; *Alkylating Agents --pharmacology--PD; *DNA Repair--drug effects--DE; *Escherichia **coli** --genetics--GE; *N-glycosyl Hydrolases--deficiency--DF; *SOS Response (Genetics)--drug effects--DE; **Adenine** --analogs and derivatives--AA; **Adenine** --metabolism--ME; Escherichia **coli** --drug effects--DE; Escherichia **coli** --enzymology--EN; Methyltransferases--metabolism--ME; Mutation; N-glycosyl Hydrolases--metabolism--ME; O(6)-Methylguanine-DNA Methyltransferase; beta-Galactosidase--metabolism--ME
CAS Registry No.: 0 (Alkylating Agents); 5142-23-4 (3-methyladenine); 73-24-5 (Adenine)
Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.63 (O(6)-Methylguanine-DNA Methyltransferase); EC 3.2.1.23 (beta-Galactosidase); EC 3.2.2.- (N-glycosyl Hydrolases); EC 3.2.2.20 (DNA-3-methyladenine glycosidase I)
Record Date Created: 19870210
Record Date Completed: 19870210

that arise as a consequence of the **Dam** - defect in a plasmid-borne phage P22 repressor gene, mnt. The majority of these mutations are A:T----G:C transitions that occur within six base pairs of the two 5'- **GATC** -3' sequences in the mnt gene. In contrast, the spectrum of mnt- mutations in a **dam** + host is comprised of a majority of insertions of IS elements and deletions that do not cluster near **Dam** recognition sites. These results show that **Dam** -directed post-replicative mismatch repair plays a significant role in the rectification of potential transition mutations in vivo, and suggest that sequences associated with **Dam** recognition sites are particularly prone to replication or repair errors.

Tags: Support, U.S. Gov't, P.H.S.

Descriptors: *DNA Repair; *Escherichia coli--genetics--GE; *Genes, Bacterial; *Methyltransferases--genetics--GE; *Mutation; Chromosome Deletion; Methylnitronitrosoguanidine; Site-Specific DNA-Methyltransferase (Adenine-Specific)

CAS Registry No.: 70-25-7 (Methylnitronitrosoguanidine)

Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific))

Record Date Created: 19870924

Record Date Completed: 19870924

2/9/44 (Item 44 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

05386069 87064422 PMID: 3023890

Restriction endonuclease activity induced by PBCV-1 virus infection of a Chlorella-like green alga.

Xia Y N; Burbank D E; Uher L; Rabussay D; Van Etten J L

Molecular and cellular biology (UNITED STATES) May 1986, 6 (5) p1430-9, ISSN 0270-7306 Journal Code: 8109087

Contract/Grant No.: GM-32441; GM; NIGMS

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

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An enzyme was isolated from a eucaryotic, Chlorella-like green alga infected with the virus PBCV-1 which exhibits type II restriction endonuclease activity. The enzyme recognized the sequence **GATC** and cleaved DNA 5' to the G. Methylation of deoxyadenosine in the **GATC** sequence **inhibited** enzyme activity. In vitro the enzyme cleaved host Chlorella nuclear DNA but not viral DNA because host DNA contains **GATC** and PBCV-1 DNA contains GmATC sequences. PBCV-1 DNA is probably methylated in vivo by the PBCV-1-induced **methyltransferase** described elsewhere (Y. Xia and J. L. Van Etten, Mol. Cell. Biol. 6:1440-1445). Restriction endonuclease activity was first detected 30 to 60 min after viral infection; the appearance of enzyme activity required de novo protein synthesis, and the enzyme is probably virus encoded. Appearance of enzyme activity coincided with the onset of host DNA degradation after PBCV-1 infection. We propose that the PBCV-1-induced restriction endonuclease participates in host DNA degradation and is part of a virus-induced restriction and modification system in PBCV-1-infected Chlorella cells.

Tags: Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Descriptors: *Algae, Green--enzymology--EN; *Cell Transformation, Viral; *DNA Restriction Enzymes--metabolism--ME; *Insect Viruses--genetics--GE; Base Sequence; Chlorella; Cycloheximide--pharmacology--PD; DNA--metabolism --ME; DNA Restriction Enzymes--isolation and purification--IP; Insect Viruses--enzymology--EN; Kinetics

CAS Registry No.: 66-81-9 (Cycloheximide); 9007-49-2 (DNA)

Enzyme No.: EC 3.1.21 (DNA Restriction Enzymes)

Record Date Created: 19870120

Record Date Completed: 19870120

2/9/4 (Item 4 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

11078198 97433340 PMID: 9287154

Specificity of DNA repair methyltransferases determined by competitive inactivation with oligonucleotide substrates: evidence that Escherichia coli Ada repairs O6-methylguanine and O4-methylthymine with similar efficiency.

Paalman S R; Sung C; Clarke N D

Department of Biophysics and Biophysical Chemistry, Johns Hopkins School of Medicine, Baltimore, Maryland 21205, USA.

Biochemistry (UNITED STATES) Sep 16 1997, 36 (37) p11118-24, ISSN 0006-2960 Journal Code: 0370623

Contract/Grant No.: CA59492; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

DNA repair methyltransferases (MTases) are stoichiometric acceptor molecules that are irreversibly **inactivated** in the course of removing a methyl group from O6-methylguanine (meG)-DNA or O4-methylthymine (meT)-DNA. A new assay has been developed to determine the relative efficiency of repair of meG and meT. The assay is based on the deprotection of methylated restriction sites in synthetic oligonucleotides and can be used to measure meG repair or meT repair directly. More importantly, relative repair efficiencies can be measured in competition experiments, using each of the methylated oligomers in turn as an **inhibitor** of repair for the other. Relative repair rates are determined by numerical solution of the coupled rate equations that describe this competition to the experimental data. We find that the human MTase repairs meT about 35-fold less well than meG, qualitatively similar to earlier studies. Contrary to previous reports, however, we find that Escherichia **coli** Ada repairs meG and meT with nearly equal efficiency. This finding, in conjunction with other recent reports, may indicate that low meT repair is a relatively unusual characteristic of the human homolog.

Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Descriptors: **Bacterial** Proteins--metabolism--ME; *DNA Repair; *Escherichia **coli** --enzymology--EN; *Methyltransferases--metabolism--ME; Bacterial Proteins--genetics--GE; Binding, Competitive; Cloning, Molecular; DNA, **Bacterial** --metabolism--ME; Escherichia **coli** --genetics--GE; Gene Expression; Guanine--analogs and derivatives--AA; Guanine--metabolism--ME; O(6)-Methylguanine-DNA Methyltransferase; Peptide Fragments--metabolism--ME ; Thymine--analogs and derivatives--AA; Thymine--metabolism--ME

CAS Registry No.: 0 (Ada regulatory protein (176-354)); 0 (Ada regulatory protein, E coli); 0 (Bacterial Proteins); 0 (DNA, Bacterial) ; 0 (Peptide Fragments); 20535-83-5 (O-(6)-methylguanine); 25902-89-0 (O-4-methylthymine); 65-71-4 (Thymine); 73-40-5 (Guanine)

Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.- (O(4)-methylthymine-DNA methyltransferase); EC 2.1.1.63 (O(6)-Methylguanine-DNA Methyltransferase)

Record Date Created: 19971014

Record Date Completed: 19971014

11348425 98228688 PMID: 9567290

[Restriction endonuclease Sse9I from Sporosarcina sp. strain 9D recognizes the 5'-AATT-3' DNA sequence]

Endonukleaza restriktsii Sse9I iz shtamma Sporosarcina sp. 9D, uznaiushchaia posledovatel'nost' DNK 5'-AATT-3'.

Gonchar D A; Dedkov V S; Verkhozina V A; Kusner Iu S; Shevchenko A V; Degtiarev S Kh

SibEnzyme, Novosibirsk, Russia.

Prikladnaia biokhimiia i mikrobiologiia (RUSSIA) Mar-Apr 1998, 34 (2) p139-41, ISSN 0555-1099 Journal Code: 0023416

Document type: Duplicate Publication; Journal Article ; English Abstract

Languages: RUSSIAN

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

A new restriction endonuclease Sse9I was isolated from the **bacterial** strain Sporosarcina sp. 9D. The enzyme belongs to Type II restrictases and recognizes the tetranucleotide sequence 5'-AATT-3'. The enzyme cleaves DNA before the first **adenine** residue, so it is a true isoschizomer of Tsp509I restrictase. However, unlike the prototype, Sse9I digests DNA at 55 degrees C and loses its activity after 20 min storage at 65 degrees C.

Descriptors: DNA--metabolism--ME; *Gram-Positive Endospore-Forming **Bacteria** --enzymology--EN; *Site-Specific DNA-Methyltransferase (**Adenine** -Specific)--metabolism--ME; Heat; Hydrolysis; Site-Specific DNA-Methyltransferase (**Adenine** -Specific)-- **antagonists** and **inhibitors** --AI; Substrate Specificity

CAS Registry No.: 9007-49-2 (DNA)

Enzyme No.: EC 2.1.1.- (DNA methyltransferase SSe9I); EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (**Adenine** -Specific))

Record Date Created: 19980508

Record Date Completed: 19980508

1408572 98290317 PMID: 9628353

Analysis of DNA methylation processes related to the inhibition **of DNA synthesis by 5-azacytidine in Streptomyces** antibioticus **ETH 7451.**

Fernandez M; Olek A; Walter J; Sanchez J

Departamento de Biologia Funcional e Instituto Universitario de Biotecnologia de Asturias, Universidad de Oviedo, Spain.

Biological chemistry (GERMANY) Apr-May 1998, 379 (4-5) p559-62, ISSN 1431-6730 Journal Code: 9700112

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

5-Azacytidine **inhibits** DNA synthesis and to a lesser proportion RNA synthesis in S. **antibioticus** . The biosynthesis of proteins is not affected. The main **inhibitory** effect of 5-azacytidine on DNA and RNA synthesis is probably caused by its incorporation into newly synthesized DNA or RNA and the formation of covalent complexes between cytosine-specific methyltransferases and the modified DNA or RNA templates. To analyze whether such effects could occur at the oriC region of S. **antibioticus** we analyzed the methylation status of this region using the bisulphite assisted genomic sequencing method. One of the cytosine residues found to be partially methylated was contained within an unique NaeI sequence (GCCGGC) in oriC. Subsequent analysis shows chromosomal DNA from S. **antibioticus** to be resistant to R.NaeI restriction indicating that this strain contains a NaeI-specific cytosine C5-methyltransferase activity. Following 5-azacytidine treatment the NaeI site within the oriC region becomes partially demethylated. Our results suggest that some of the 5-azacytidine effects on DNA and RNA synthesis might indeed be related to the complex formation and **inhibition** of a cytosine-specific DNA

pp2

STRAIN=Classical Ogawa 395 / ATCC 39541 / Serotype O1;
MEDLINE=21562622; PubMed=11705940; [NCBI, ExPASy, EBI, Israel, Japan]
Julio S.M., Heithoff D.M., Provenzano D., Klose K.E., Sinsheimer R.L., Low D.A., Mahan M.J.;
"DNA adenine methylase is essential for viability and plays a role in the pathogenesis of Yersinia pseudotuberculosis and Vibrio cholerae.";
Infect. Immun. 69:7610-7615(200

STRAIN=Nichols;
MEDLINE=98005685; PubMed=9345771; [NCBI, ExPASy, EBI, Israel, Japan]
Stamm L.V., Greene S.R., Barnes N.Y., Bergen H.L., Hardham J.M.;
"Identification and characterization of a Treponema pallidum subsp. pallidum gene encoding a DNA adenine methyltransferase.";
FEMS Microbiol. Lett. 155:115-119(1997).
[2]
SEQUENCE FROM NUCLEIC ACID.
STRAIN=Nichols;
MEDLINE=98332770; PubMed=9665876; [NCBI, ExPASy, EBI, Israel, Japan]
Fraser C.M., Norris S.J., Weinstock G.M., White O., Sutton G.G., Dodson R., Gwinn M., Hickey E.K., Clayton R., Ketchum K.A., Sodergren E., Hardham J.M., McLeod M.P., Salzberg S.,
Peterson J., Khalak H., Richardson D., Howell J.K., Chidambaram M., Utterback T., McDonald L., Artiach P., Bowman C., Cotton M.D., Fujii C., Garland S., Hatch B., Horst K., Roberts K.,
Sandusky M., Weidman J., Smith H.O., Venter J.C.;
"Complete genome sequence of Treponema pallidum, the syphilis spirochete.";
Science 281:375-388(1998).

SEQUENCE FROM NUCLEIC ACID.
STRAIN=Sr41;
MEDLINE=99315777; PubMed=10383952; [NCBI, ExPASy, EBI, Israel, Japan]
Ostendorf T., Cherepanov P., de Vries J., Wackernagel W.;
"Characterization of a dam mutant of Serratia marcescens and nucleotide sequence of the dam region.";
J. Bacteriol. 181:3880-3885(1999).

STRAIN=WR302;
MEDLINE=97465963; PubMed=9321671; [NCBI, ExPASy, EBI, Israel, Japan]
Gunn J.S., Stein D.C.;
"The Neisseria gonorrhoeae S.NgoVIII restriction/modification system: a type IIs system homologous to the Haemophilus parahaemolyticus HphI restriction/modification system.";
Nucleic Acids Res. 25:4147-4152(1997).

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QR1.F4 adams

STRAIN=Classical Ogawa 395 / ATCC 39541 / Serotype O1;
MEDLINE=21562622; PubMed=11705940; [NCBI, ExPASy, EBI, Israel, Japan]
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Infect. Immun. 69:7610-7615(200

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MEDLINE=98332770; PubMed=9665876; [NCBI, ExPASy, EBI, Israel, Japan]
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Peterson J., Khalak H., Richardson D., Howell J.K., Chidambaram M., Utterback T., McDonald L., Artiach P., Bowman C., Cotton M.D., Fujii C., Garland S., Hatch B., Horst K., Roberts K.,
Sandusky M., Weidman J., Smith H.O., Venter J.C.;
"Complete genome sequence of Treponema pallidum, the syphilis spirochete.";
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MEDLINE=99315777; PubMed=10383952; [NCBI, ExPASy, EBI, Israel, Japan]
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"Characterization of a dam mutant of Serratia marcescens and nucleotide sequence of the dam region.";
J. Bacteriol. 181:3880-3885(1999).

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MEDLINE=97465963; PubMed=9321671; [NCBI, ExPASy, EBI, Israel, Japan]
Gunn J.S., Stein D.C.;
"The Neisseria gonorrhoeae S.NgoVIII restriction/modification system: a type IIs system homologous to the Haemophilus parahaemolyticus HphI restriction/modification system.";
Nucleic Acids Res. 25:4147-4152(1997).

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Mechanism and control of interspecies recombination in Escherichia coli. I. Mismatch repair, methylation, recombination and replication functions.

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Genetics (UNITED STATES) Oct 1998, 150 (2) p533-42, ISSN 0016-6731 Journal Code: FNH

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Subfile: INDEX MEDICUS

A genetic analysis of interspecies recombination in Escherichia coli between the linear Hfr DNA from **Salmonella** typhimurium and the circular recipient chromosome reveals some fundamental aspects of recombination between related DNA sequences. The MutS and **MutL** mismatch binding proteins edit (prevent) homeologous recombination between these 16% diverged genomes by at least two distinct mechanisms. One is MutH independent and presumably acts by aborting the initiated recombination through the UvrD helicase activity. The RecBCD nuclease might contribute to this editing step, presumably by preventing reiterated initiations of recombination at a given locus. The other editing mechanism is MutH dependent, requires unmethylated GATC sequences, and probably corresponds to an incomplete long-patch mismatch repair process that does not depend on UvrD helicase activity. Insignificant effects of the **Dam** methylation of parental DNAs suggest that unmethylated GATC sequences involved in the MutH-dependent editing are newly synthesized in the course of recombination. This hypothetical, recombination-associated DNA synthesis involves PriA and RecF functions, which, therefore, determine the extent of MutH effect on interspecies recombination. Sequence divergence of recombining DNAs appears to limit the frequency, length, and stability of early heteroduplex intermediates, which can be stabilized, and the recombinants mature via the initiation of DNA replication.

Tags: Support, Non-U.S. Gov't

Descriptors: *Escherichia coli--genetics--GE; *Models, Genetic; *Recombination, Genetic--genetics--GE; Bacterial Proteins--genetics--GE; Bacterial Proteins--physiology--PH; Crosses, Genetic; DNA Helicases --physiology--PH; DNA Methylation; DNA Repair--genetics--GE; DNA Replication--genetics--GE; DNA-Binding Proteins--genetics--GE; DNA-Binding Proteins--physiology--PH; Mutation; **Salmonella** typhimurium--genetics--GE; Serine Endopeptidases--genetics--GE; Serine Endopeptidases--physiology--PH ; Site-Specific DNA-Methyltransferase (Adenine-Specific)--genetics--GE; Site-Specific DNA-Methyltransferase (Adenine-Specific)--physiology--PH

CAS Registry No.: 0 (Bacterial Proteins); 0 (DNA-Binding Proteins); 0 (MutL protein); 0 (MutS protein); 0 (RP-A protein); 0 (lexA protein) ; 93230-16-1 (recF protein)

Enzyme No.: EC 2.1.1.- (**Dam** methyltransferase); EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific)); EC 3.4.21 (Serine Endopeptidases); EC 5.99.- (DNA Helicases)

Record Date Created: 19981116